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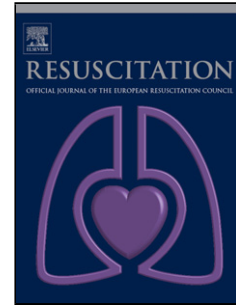
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1 **TITLE PAGE**

2

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6

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31

1 **ABSTRACT**

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

5 Here we investigated if progression of auditory discrimination can predict cognitive and
6 functional outcome.

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

13 **Results:** Thirty-two patients were included, 14 “predicted survivors” and 18 “other survivors”.
14 “Predicted survivors” were more likely to recover basic cognitive functions shortly after
15 awakening (ability to follow a standardized neuropsychological battery: 86% vs. 44%; $p=0.03$
16 (Fisher)) and to show a very good functional outcome at 3 months (CPC 1: 86% vs. 33%;
17 $p=0.004$ (Fisher)). Moreover, progression of auditory discrimination during coma was strongly
18 correlated with cognitive performance on awakening (phonemic verbal fluency: $r_s=0.48$; $p=0.009$
19 (Spearman)).

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

1

2 INTRODUCTION

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

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

1 difference informative of survivors' functional outcome? (2) Is the degree of improvement
2 indicative of the degree of recovery?

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

12

1 METHODS

2 Study design and population

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

10

11 All but five patients were treated with mild therapeutic hypothermia to 33-34°C for the first 24
12 hours, induced through ice packs and the Arctic Sun® system surface cooling device
13 (Medivance, Louisville, CO, USA), in agreement with current guidelines¹⁷. Midazolam (0.1
14 mg/kg/h) and fentanyl (1.5 μ g/kg/h) were given for sedation-analgesia, and vecuronium (0.1
15 mg/kg boluses) in case of shivering. Patients with myoclonus or electrographic epileptic seizures
16 received intravenous, nonsedating anti-epileptic treatment (valproate, levetiracetam). Return to
17 normal temperature was controlled at 0.5°C increase per hour until 37°C. Sedation was
18 discontinued at 36°C. Four out of the five patients not receiving therapeutic hypothermia had
19 targeted temperature management at 36°C for 24h, the remaining patient had no temperature
20 control; all were sedated as the hypothermic patients. The decision to prescribe hypothermia was
21 taken according to patient's clinical situation and following latest recommendations¹⁸. On the
22 second day, all patients were normothermic.

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

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

9

10 **Mismatch Negativity paradigm**

11 As described in details in a previous study ¹⁰, we used an auditory MMN paradigm including one
12 standard and three types of deviant sounds (pitch, duration and location deviants). Stimuli were
13 separated by a constant interval of 950 ms between the onsets of two sounds. Standards were
14 1000 Hz sinusoidal tones of 100 ms duration and 0 ms inter-aural time difference. Pitch deviants
15 were at 1200 Hz, duration deviants lasted 150 ms, and location deviants had 700 ms inter-aural
16 time difference (left ear leading). Standard sounds were presented in 70%, while each type of
17 deviant was presented in 10% of trials. A sequence included 500 standard sounds and 50 of each
18 type of deviant sounds organized in a pseudo-random order. The same sequence was used in
19 three consecutive blocks. Auditory stimuli were displayed at 90dB via specialized ER4 Etymotic
20 earphones (Etymotic Research, Inc.) using E-prime 2.0 software for patients included up to 2014
21 (Psychology Software Tools Inc., Pittsburgh, PA) or the Psychophysics Toolbox (Psychtoolbox-
22 3) extensions in Matlab ²⁰⁻²². The procedure was identical for recordings on the first and second
23 day of coma.

1

2 **EEG acquisition and pre-processing**

3 EEG recordings were performed as detailed previously^{19,23} using a 19 electrodes montage
4 following the international 10-20 system (Viasys Neurocare, Madison, WI, USA; sampling rate
5 of 1024 Hz, online reference to Fpz). For each patient, two recordings were collected: on the first
6 day after admission, during hypothermia or normothermia but always under active sedation, and
7 on the second day of coma, during normothermic conditions (at least 35°C), after sedation
8 weaning. The recording included the MMN paradigm, run after the routine clinical part lasting
9 20-30 minutes^{10,11}.

10 Preprocessing was performed using Cartool v.3.43²⁴. We extracted peri-stimulus epochs
11 spanning 50 ms before to 500 ms post-stimulus onset. An artefact rejection criterion of $\pm 100 \mu\text{V}$
12 was applied offline. Data were re-referenced offline to the common average reference, 0.18–40
13 Hz band-pass filtered, and 50 Hz notch filtered. No prestimulus baseline correction was applied.

14

15 **Decoding of single-trial EEG**

16 As in our previous studies, we analysed auditory evoked responses to standard and deviant
17 sounds using a multivariate EEG analysis²⁵⁻²⁷, extracting in a data-driven manner time periods
18 and prototypical voltage topographies discriminating between the two conditions. This offers the
19 advantage of being free of *a priori* hypotheses about electrode location where a stimulus-related
20 activity would be expected, and is independent of any inclusion criteria aside from having
21 sufficient artifact-free trials. Because this method is based on voltage topographies, an accurate
22 performance results from activation of different underlying neural generators between
23 experimental conditions²⁶.

7

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

10

11 **Early cognitive functioning**

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

19

20 **Functional outcome**

21 Long-term global outcome was assessed using the Cerebral Performance Categories scale (CPC;
22 Booth, Boone, Tomlinson, & Detsky, 2004) at 3 months follow-up through a short semi-
23 structured phone interview by a research nurse blinded both to auditory discrimination and

1 cognitive testing. Outcomes categorized as “very good” for CPC 1 and “moderate” for CPC 2-3;
2 no patient was vegetative (CPC 4).

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

9

10 **Relation between progression of auditory discrimination and outcome**

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

16

1 **RESULTS**

2 **Auditory discrimination results during coma**

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

10

11 **Cognitive functioning on awakening**

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

17

18 **Functional outcome**

19 At 3 months follow-up, 18 (56%) patients showed very good (CPC 1) and 13 (41%) moderate
20 recovery (ten with CPC 2, three with CPC 3); one died few weeks after awakening (CPC 5) after
21 decision to provide palliative care in a poor prognosis context related to severe comorbidities.
22 Among the 20 patients who completed the whole neuropsychological examination on awakening,
23 16 (80%) had a CPC 1 and four (20%) a CPC 2; there was no patient with CPC 3. In comparison,

10

1 only two (17%) out of the 12 patients who could not complete the neuropsychological
2 assessment on awakening had a CPC 1; six (50%) had a CPC 2, three (25%) a CPC 3 and one
3 (8%) died. The proportion of patients with very good recovery (CPC 1) vs. moderate recovery
4 (CPC 2-3) was significantly different in these two groups ($p = 0.002$; Fischer exact test).

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

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

12

13 **Relation between progression of auditory discrimination and outcome**

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

1 -0.4, $p = 0.03$; hospital stay duration: $r_s = -0.49$, $p = 0.006$). No such significant relationship was
2 found for digit span forward scores.

3

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

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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 death⁴. 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

1 undergo the whole neuropsychological testing and orientation to time were interesting variables,
2 reflecting the recovery of basic cognitive functions. In addition, the strong relationship between
3 the ability to complete the whole neuropsychological assessment and CPC scores at three months
4 suggests that early cognitive evaluation can be seen as a predictor of subsequent functional
5 recovery, confirming results from previous studies ^{6,32}. Verbal fluency represents a complex
6 measure covering multiple cognitive domains, including primarily executive functions (e.g. self
7 initiation, switching, inhibition), and verbal abilities ³³. Semantic and phonemic verbal fluency
8 differ regarding both the involved neuroanatomical substrates and the recruited cognitive
9 processes, with more executive processes and frontal involvement in phonemic verbal fluency
10 ^{34,35}. Combined together, we believe that these measures may constitute a global and
11 parsimonious appreciation of cognitive functioning, which could be easily used in routine
12 clinical evaluations to quickly assess patient's status. In addition, testing cognition shortly after
13 awakening may have several advantages: influence of motivational and environmental factors
14 that might appear later in time (e.g. external stimulations, targeted neurorehabilitative treatments)
15 is reduced and there is less chance to lose patients at follow-up; moreover, early
16 neuropsychological examination is of clinical value in the decision for appropriate treatments.
17 Considering that the aim here was to determine if auditory discrimination during coma is related
18 with cognitive functions at all, we feel that the present setting allows assessing more directly the
19 relationship between acute cerebral processing and subsequent cognitive functioning in two
20 groups of survivors with strictly identical conditions.

21

22 In contrast to previous outcome studies characterizing good outcome as CPC 1-2 and poor
23 outcome as CPC 3-5 ⁴, here our cohort included only survivors with CPC 1-3 (there were no

1 vegetative state patients at three months). As our aim was to predict very good outcome, we
2 considered separately patients having no or minor neurological deficits (CPC 1) and the rest
3 (CPC 2-3) as moderate. Combined with the fact that inter-rater variability³⁶ was not an issue as
4 the same research nurse collected all CPC scores, we believe that this classification provides
5 accurate information for our purpose. Even though coma and hospital stay durations can be
6 influenced by many factors besides brain injury (e.g., infectious or cardiovascular
7 complications), they proved to be consistent with other measures and reliable indicators of the
8 recovery speed. In particular, the tendency of “other survivors” to undergo neuropsychological
9 testing later, while still having worse cognitive performance, suggests that longer time to recover
10 is indicative of poor outcome. In fact, coma duration has been previously associated with
11 functional status, showing more complaints of cognitive functioning and worse quality of life in
12 patients awakening later^{37,38}. Indication to intensive neurorehabilitative treatment was also a
13 marker of poor outcome.

14
15 Interestingly, cardiac arrest duration tended to be shorter in “predicted survivors”, suggesting
16 that a briefer insult correlates to a better recovery of brain functions assessed by progression of
17 auditory discrimination. In previous studies, arrest duration has been related to survival³⁹, but, as
18 far as we are aware, never with detailed outcome^{40,41}, except in one older report showing a
19 significant association with long-term memory scores⁴². To the best of our knowledge, our study
20 is the first to suggest that patients recovering auditory functions during coma (and later
21 exhibiting better outcome) have lighter initial insult as attested by shorter time to ROSC.

22

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

18
19

20 **CONCLUSIONS**

21 Progression of auditory discrimination over time during early coma seems to reliably predict the
22 subsequent cognitive and functional outcome of cardiac arrest survivors. These findings, together
23 with the consideration of time to ROSC and to extubation, may orient relatively early the clinical
24 teams and proxy regarding the management of rehabilitation care. Confirmation of these results

- 1 for detailed long-term outcome prediction in a larger cohort could contribute to more accurately
- 2 orient early rehabilitation efforts and therefore improve patients' outcome.

1

2 Conflicts of interest

3 The authors declare no conflict of interest.

4

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12

13 Author contributions

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

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24
25

1 **FIGURE LEGENDS**

2

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

5 *MMN* Mismatch Negativity; *CPC* Cerebral Performance Category

6

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

12

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

19

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

23

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

6

	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

1

2

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

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

7 * Significant at $p < 0.05$

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

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

24

1 ¥ Scores available for 31 patients (14 predicted survivors / 17 other survivors)

2

3 Cardiac arrest survivors were split in two groups according to the progression of auditory
4 discrimination during coma (“predicted survivors” vs. “other survivors”) and compared on
5 several measures using appropriate statistical tests.

6 Detailed CPC results: in the “predicted survivors” group, two patients (14%) had a CPC 2 and no
7 patient (0%) had a CPC 3; in the “other survivors” group, eight patients (44%) had a CPC 2,
8 three (17%) had a CPC 3 and one died.

9

Figure 1

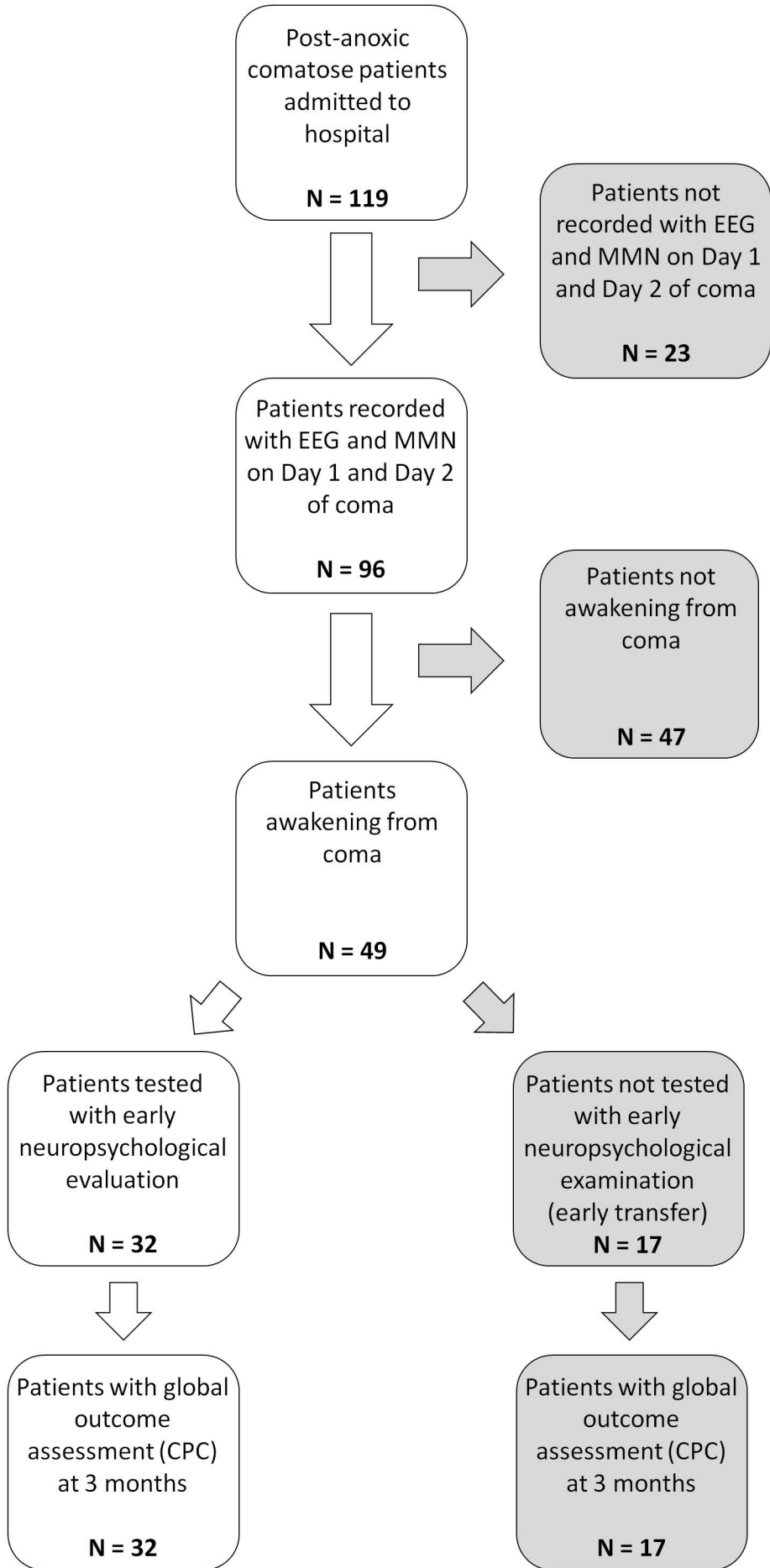


Figure 2

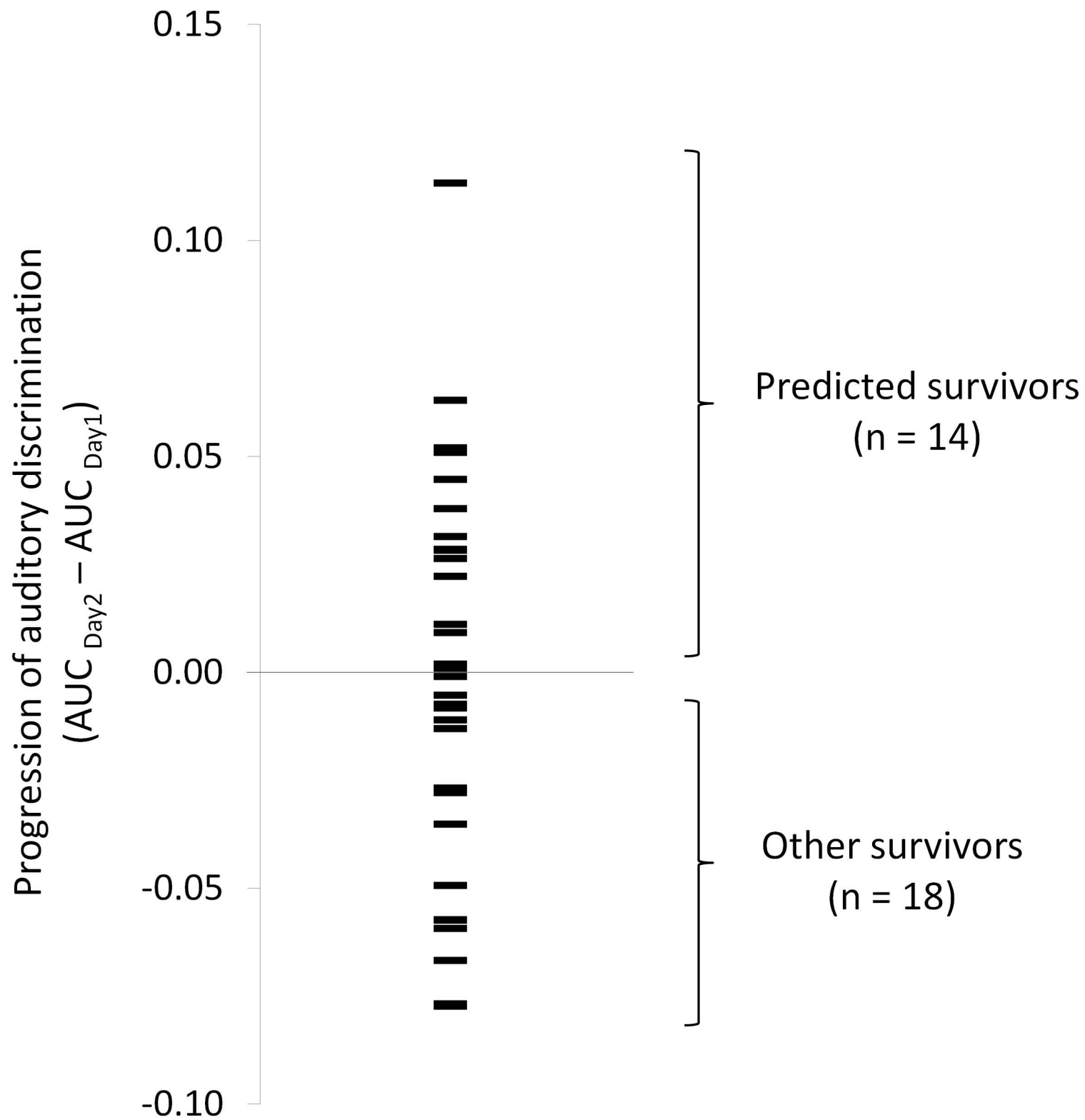


Figure 3

Overall results of the neuropsychological assessment on awakening for each cognitive domain

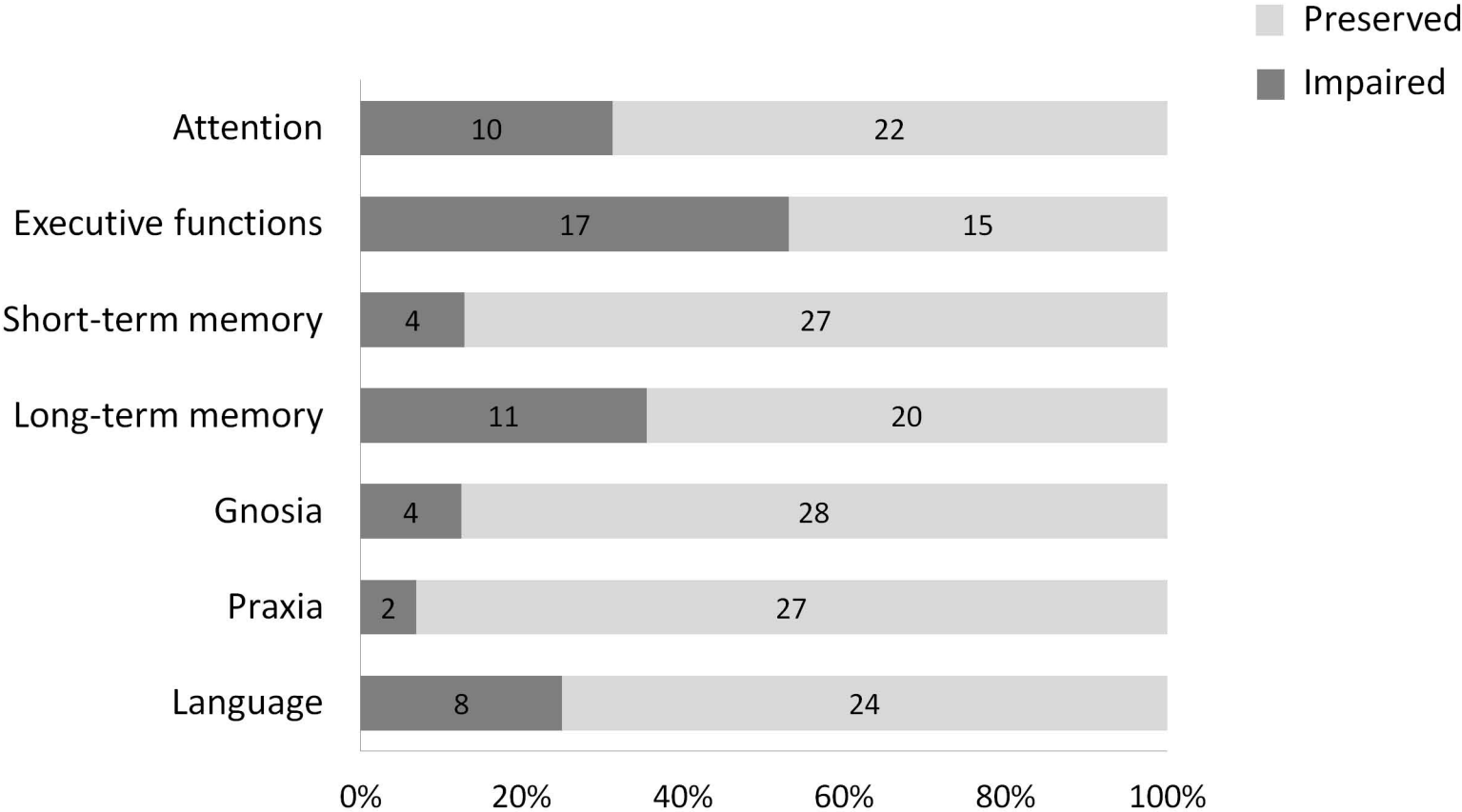


Figure 4

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

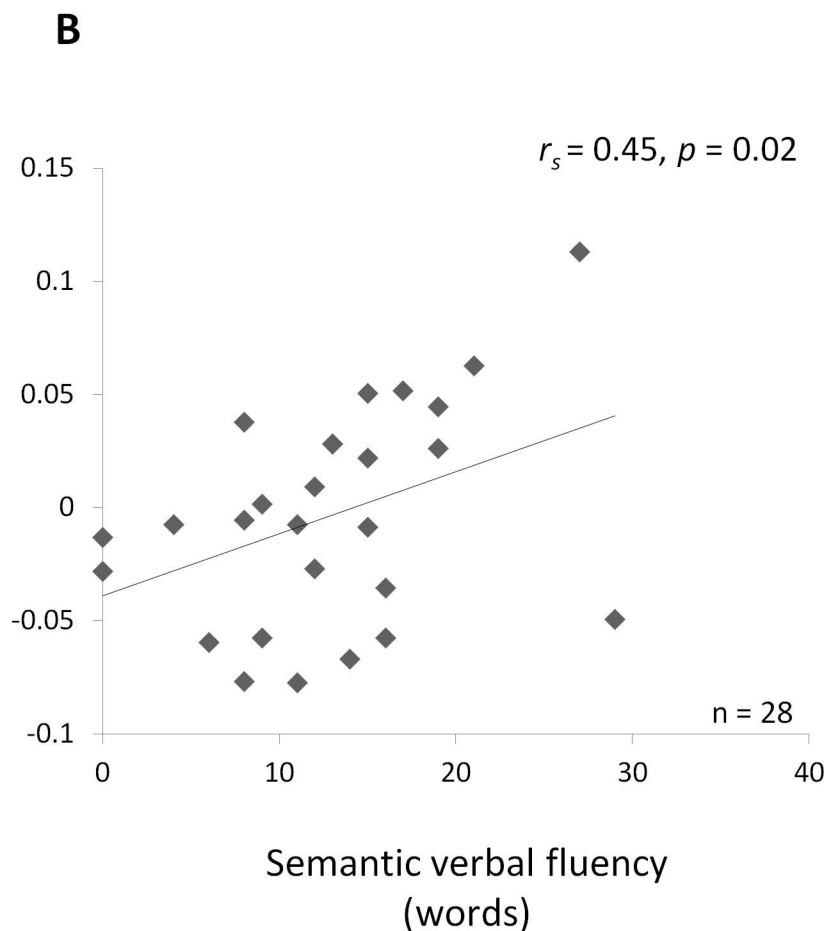
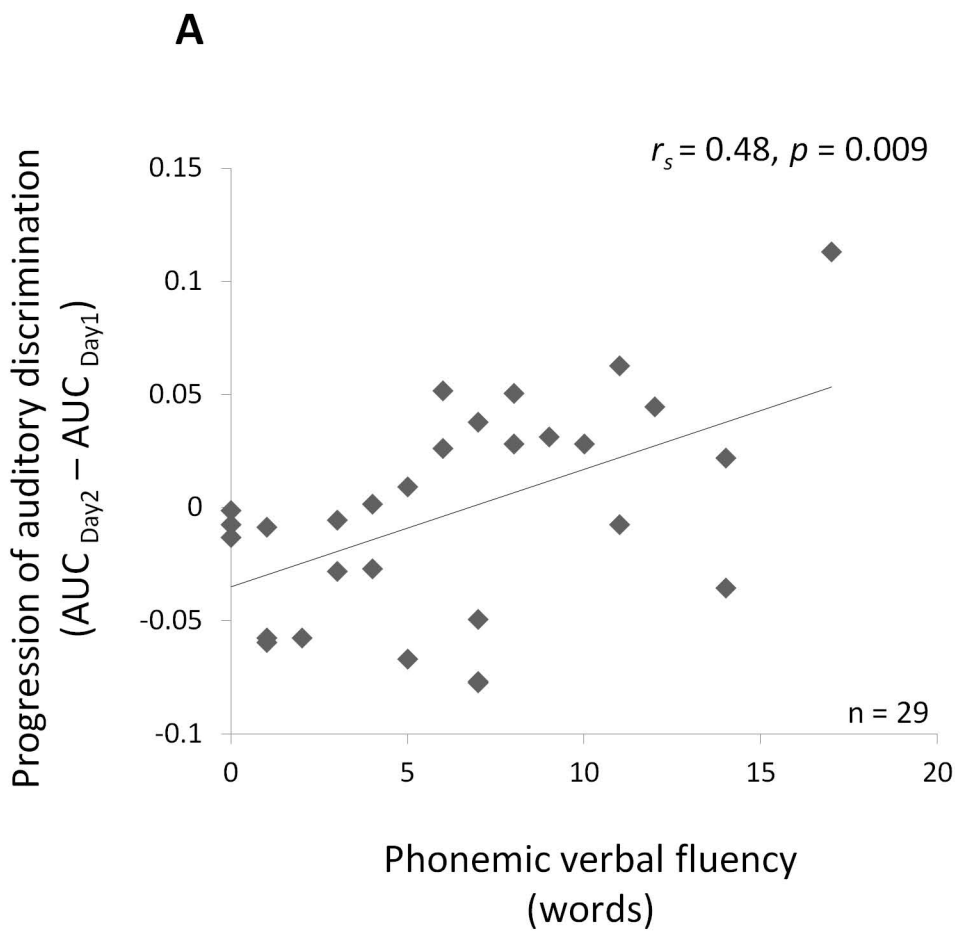


Figure 5

Correlation between progression of auditory discrimination during coma and functional outcome

