Appendix.

Clinical sketches of patients whose clinical diagnosis improved.

Case 1. A 61-year-old female was enrolled for selegiline study in minimally conscious state minus (MCS-) showing ability of object manipulation (CRS-R total score: 9) 13 months after a severe right nucleo-capsular haemorrhage with intraventricular extension. At 3-week selegiline administration, she evolved in MCS plus (MCS+), since she recovered reproducible movements to command (CRS-R total score: 12). At 5-week selegiline administration, she further recovered intelligible verbalization and intentional, but not functional, communication, but her clinical diagnosis was not changed (CRS-R total score: 14). At 10-week selegiline administration, she recovered also functional and appropriate non-verbal communication abilities and ability to distinguish two different objects, thus emerging from MCS+ (CRS-R total score: 20). During the 4 weeks after selegiline withdrawal, these clinical improvements persisted.

Case 2. A 59-year-old female acutely developed a comatose state due to a severe right fronto- temporo-parietal brain haemorrhage with compression of the ventricles and shift of the 3rd ventricle and septum pellucidum to the opposite site, due to aneurysm rupture of arteria cerebri days later. Nine months since brain injury, she was enrolled in the study, when she was in stabilized clinical condition of MCS-, showing object manipulation only, as confirmed by repeated (in 4 weeks) and accurate clinical evaluations with best score of CRS-R total score of 9. At 3-week selegiline administration, she showed a transient worsening in clinical diagnosis (from MCS- to VS; CRS-R: 5), likely related to 3 days of hyperthermia due to urinary tract infection. She regained ability of object manipulation in one week. After 6 weeks of selegiline media.

She underwent a decompressive craniectomy and then was diagnosed to be in VS 20 days later. Nine months since brain injury, she was enrolled in the study, when she was in stabilized clinical condition of MCS-, showing object manipulation only, as confirmed by repeated (in 4 weeks) and accurate clinical evaluations with best score of CRS-R total score of 9. At 3-week selegiline administration, she showed a transient worsening in clinical diagnosis (from MCS- to VS; CRS-R: 5), likely related to 3 days of hyperthermia due to urinary tract infection. She regained ability of object manipulation in one week. After 6 weeks of selegiline administration, she recovered reproducible movements to command, visual pursuit, ability of reaching objects and non-functional communication thus progressing to MCS+ (CRS-R total score: 13). These clinical improvements persisted during the 4 weeks after selegiline withdrawal.

Case 3. A 24 year-old male was enrolled for selegiline study in MCS+ 8 months after a severe subarachnoid haemorrhage with right fronto-parieto-temporal lesions, caused by aneurysm rupture. At study entry he showed visual pursuit and reproducible eye movements to non- object related commands, such as “look up at ceiling, look down at floor” (CRS-R total score: 9). After 1 week of selegiline administration he presented flexion withdrawal to noxious stimuli and an increase in arousal sub-scale (CRS-R total score: 11). After 4 weeks of selegiline administration, he recovered object recognition and clearly discernible non-verbal (eye-coded) non-functional communicative responses (CRS-R total score: 13). After 5 weeks he showed a transient (5 days) deterioration of clinical status from MCS+ to VS, due to pneumonia.

After 8 weeks of selegiline administration, he emerged from MCS+, since he regained functional and accurate non-verbal (eye-coded) communicative responses (CRS-R total score: 16). No further clinical changes occurred during the follow-up period.

Case 4. A 63 year-old male was enrolled for selegiline study 6 months after a severe and extensive right temporo-parietal brain haemorrhage, with intraventricular involvement and trans-tentorial herniation. At study entry he was in VS (CRS-R total score: 4), but after 2 weeks of selegiline administration he showed an increase in arousal level and then recovered reproducible eye and right hand movements to command and flexion withdrawal to nociceptive stimuli, thus evolving to MCS+ (CRS-R total score: 9). However, selegiline administration had to be stopped after 4 weeks, because of persistent supraventricular tachycardia. One week after withdrawal the patient showed a transient mild deterioration of his response to noxious stimuli (CRS-R total score: 8) with abnormal posturing, without change in clinical diagnosis. Four weeks after selegiline withdrawal, the patient was still in MCS+ and continued to present episodic sinus tachycardia, sometimes clearly related to noxious stimuli.