

Supplementary Material

Narrative clinical histories for the patients with evidence of covert command following on fMRI:

Patient 1. At the age of 22, this young woman suffered idiopathic basilar artery occlusion resulting in ischemic injury in the ventral pons, tegmental midbrain, bilateral thalami, right calcarine cortex and bilateral (left greater than right) entorhinal cortices. She had no prior medical history, known risk factors for thromboembolic or vascular disorders or history of substance abuse. She was taking oral contraceptives at the time of the stroke. She underwent intraarterial thrombolytic treatment, which resulted in restored blood flow of the vertebrobasilar system but residual ischemic lesions in the territory of the posterior circulation persisted (as detailed above). She was transferred to a rehabilitation hospital 3 weeks after the event, when she was described to be unconscious with no spontaneous eye opening. Within the next month she demonstrated partial left eye opening, and within 3 months partial, bilateral eye opening. At that time, she was able to moan intermittently, but did not demonstrate any evidence of purposeful movements with the exception of stereotyped, repetitive left second finger movements; therefore she was diagnosed to be in vegetative state. At 4 months post-injury she was reported to

demonstrate possible context related purposeful behaviors including cry-like vocalizations in response to emotional conversations, humming vocalization in response to singing, and slight movements of her head toward conversations and away from noxious stimulation, however her behavioral diagnosis did not change. It was during her first evaluation by our research team at nearly 2 years after the brain injury that she was found to be able to intermittently follow commands using small amplitude vertical left eye movements; therefore, she was diagnosed to be in minimally conscious state. Over the next 4 years, she continued to receive intensive physical, occupation and speech therapy; however, her ability to answer yes/no questions remained inconsistent and highly dependent on level of alertness. Currently she is participating in an intensive program to develop a personalized brain-computer interface utilizing her left eye movements as a response but reliable communication channel has not yet been established.

Patient 2. At the age of 23, this man suffered severe traumatic brain injury after hitting a pole while driving his car. He was initially reported to be able to respond to questions in the emergency room, but then lost consciousness and had prolonged hospitalization requiring right sided craniotomy, tracheostomy and percutaneous entero-gastrostomy. He was in coma for about 1 month following the injury, when he started to open his eyes spontaneously and was diagnosed to be in vegetative state. Later, his course was complicated by severe autonomic instability with tachycardia and high fevers. About 4 months after the injury, he was noted to have possible brief periods of visual fixation and tracking. He received intensive rehabilitation with steady improvement in his alertness,

however, it was about a 6 months after his injury when his therapist discovered that he was able to effectively communicate using head nods and a letter board, and he was diagnosed to be emerged from minimally conscious state. 2 years after the accident he had full neuropsychological evaluation and found to have normal intelligence. Later, he began to use a special device connected to a computer to communicate, including writing emails. He continued to have intensive speech therapy over the next couple years and about 7 years after his injury he vocalized a single word for the first time since the accident.

Patient 3. At the age of 18, this young female patient suffered severe traumatic brain injury after falling off from the hood of a motor vehicle. At the scene she was found to be comatose and she was intubated. Brain imaging revealed epidural hemorrhage and she underwent emergent left-sided craniectomy. About a month later, she also received right-sided craniectomy for difficult-to-control increased intracranial pressure and subsequent worsening tonsillar and subfalcine herniation. Two months after the injury, she had a ventriculo-peritoneal shunt placed. Five months after the accident, she underwent a left sided, and 3 months later, right-sided cranioplasty. Following the cranioplasties, her alertness improved significantly and about 10 months after the brain injury she had evidence for command following using right hand squeezing as a response and intermittent ability to communicate. Her hospital course was complicated by intracranial fluid collection and infection under the cranioplasty. About 12 months after her brain injury she developed multi-organ failure, septic shock and died.

Patient 4. At the age of 19, this patient suffered severe traumatic brain injury after he fell backwards while skateboarding and not wearing a helmet. Acute brain imaging showed diffuse subarachnoid hemorrhage, multi-focal intracranial hemorrhage, bilateral frontal and temporal contusion and right-sided subdural hemorrhage with tonsillar herniation. He underwent bilateral craniotomy for hematoma evacuation and subsequently received ventriculo-parietal shunt, tracheostomy and percutaneous entero-gastrostomy. He was consistently diagnosed to be in vegetative state for four years as he was not able to move any of his extremities, not able to open or move his eyes and could not speak or vocalize. 4 years after his accident, an occupational therapist discovered by chance that he can control the fall of his upright hand and is able to answer yes/no questions by touching either his head or abdomen as a response. This method required significant contribution by the therapist to initiate the fall of the hand. His command following and communication abilities were confirmed only after careful examination by our research team. These evaluations were performed while arm holder was blindfolded and had noise-cancellation headphones to minimize all possible biases. An individualized quantitative behavioral assessment (IQBA) questionnaire which utilized autobiographical, logical and orientation questions revealed overall accuracy of 61% of correct answers to yes/no questions with individual sessions yielding up to 88% accuracy.

Supplementary Material

Narrative clinical histories for the patients with evidence of covert command following on fMRI:

Patient 1. At the age of 22, this young woman suffered idiopathic basilar artery occlusion resulting in ischemic injury in the ventral pons, tegmental midbrain, bilateral thalami, right calcarine cortex and bilateral (left greater than right) entorhinal cortices. She had no prior medical history, known risk factors for thromboembolic or vascular disorders or history of substance abuse. She was taking oral contraceptives at the time of the stroke. She underwent intraarterial thrombolytic treatment, which resulted in restored blood flow of the vertebrobasilar system but residual ischemic lesions in the territory of the posterior circulation persisted (as detailed above). She was transferred to a rehabilitation hospital 3 weeks after the event, when she was described to be unconscious with no spontaneous eye opening. Within the next month she demonstrated partial left eye opening, and within 3 months partial, bilateral eye opening. At that time, she was able to moan intermittently, but did not demonstrate any evidence of purposeful movements with the exception of stereotyped, repetitive left second finger movements; therefore she was diagnosed to be in vegetative state. At 4 months post-injury she was reported to demonstrate possible context related purposeful behaviors including cry-like vocalizations in response to emotional conversations, humming vocalization in

response to singing, and slight movements of her head toward conversations and away from noxious stimulation, however her behavioral diagnosis did not change.

It was during her first evaluation by our research team at nearly 2 years after the brain injury that she was found to be able to intermittently follow commands using small amplitude vertical left eye movements; therefore, she was diagnosed to be in minimally conscious state. Over the next 4 years, she continued to receive intensive physical, occupation and speech therapy; however, her ability to answer yes/no questions remained inconsistent and highly dependent on level of alertness. Currently she is participating in an intensive program to develop a personalized brain-computer interface utilizing her left eye movements as a response but reliable communication channel has not yet been established.

Patient 2. At the age of 23, this man suffered severe traumatic brain injury after hitting a pole while driving his car. He was initially reported to be able to respond to questions in the emergency room, but then lost consciousness and had prolonged hospitalization requiring right sided craniotomy, tracheostomy and percutaneous entero-gastrostomy. He was in coma for about 1 month following the injury, when he started to open his eyes spontaneously and was diagnosed to be in vegetative state. Later, his course was complicated by severe autonomic instability with tachycardia and high fevers. About 4 months after the injury, he was noted to have possible brief periods of visual fixation and tracking. He received intensive rehabilitation with steady improvement in his alertness, however, it was about a 6 months after his injury when his therapist discovered that he was able to effectively communicate using head nods and a letter board,

and he was diagnosed to be emerged from minimally conscious state. 2 years after the accident he had full neuropsychological evaluation and found to have normal intelligence. Later, he began to use a special device connected to a computer to communicate, including writing emails. He continued to have intensive speech therapy over the next couple years and about 7 years after his injury he vocalized a single word for the first time since the accident.

Patient 3. At the age of 18, this young female patient suffered severe traumatic brain injury after falling off from the hood of a motor vehicle. At the scene she was found to be comatose and she was intubated. Brain imaging revealed epidural hemorrhage and she underwent emergent left-sided craniectomy. About a month later, she also received right-sided craniectomy for difficult-to-control increased intracranial pressure and subsequent worsening tonsillar and subfalcine herniation. Two months after the injury, she had a ventriculo-peritoneal shunt placed. Five months after the accident, she underwent a left sided, and 3 months later, right-sided cranioplasty. Following the cranioplasties, her alertness improved significantly and about 10 months after the brain injury she had evidence for command following using right hand squeezing as a response and intermittent ability to communicate. Her hospital course was complicated by intracranial fluid collection and infection under the cranioplasty. About 12 months after her brain injury she developed multi-organ failure, septic shock and died.

Patient 4. At the age of 19, this patient suffered severe traumatic brain injury after he fell backwards while skateboarding and not wearing a helmet. Acute brain imaging showed diffuse subarachnoid hemorrhage, multi-focal intracranial hemorrhage, bilateral frontal and temporal contusion and right-sided subdural hemorrhage with tonsillar herniation. He underwent bilateral craniotomy for hematoma evacuation and subsequently received ventriculo-parietal shunt, tracheostomy and percutaneous entero-gastrostomy. He was consistently diagnosed to be in vegetative state for four years as he was not able to move any of his extremities, not able to open or move his eyes and could not speak or vocalize. 4 years after his accident, an occupational therapist discovered by chance that he can control the fall of his upright hand and is able to answer yes/no questions by touching either his head or abdomen as a response. This method required significant contribution by the therapist to initiate the fall of the hand. His command following and communication abilities were confirmed only after careful examination by our research team. These evaluations were performed while arm holder was blindfolded and had noise-cancellation headphones to minimize all possible biases. An individualized quantitative behavioral assessment (IQBA) questionnaire which utilized autobiographical, logical and orientation questions revealed overall accuracy of 61% of correct answers to yes/no questions with individual sessions yielding up to 88% accuracy.