Supplementary Appendix A

PS 1 was a 25-year-old man who suffered a severe head injury in a motor vehicle accident two years prior to the study. Initial treatment was supportive. He remained comatose for approximately 4 weeks before transitioning to vegetative state (VS). 3 months post-injury he showed evidence of awareness of environment through visual tracking. At the time of study, 25 months post-injury, he was considered to be in a locked-in state (LIS) as he could communicate with yes / no responses via blinks or side-to-side head movements. Otherwise, his brain injury and peripheral contractures left him unable to vocalize or gesture. At the time of the study PS 1 was taking escitalopram, bromocriptine and baclofen.

PS 2 was a 19-year-old woman who sustained a severe head injury from a fall. The fall resulted in a left epidural hematoma complicated by cerebral edema with central herniation, and an initial Glasgow Coma Scale (Teasdale and Jennett, 1974) was 3. During the hospitalization from the injury, the hematoma was evacuated and bilateral craniectomies were performed to relieve increased intracranial pressure. This was followed by a 5-month period of inconsistent evidence of responsiveness as documented in medical records. The patient then underwent a left-sided cranioplasty, with subsequent recovery of ability to follow simple motor commands. 6 months after injury, our first study was performed. At that time, the right craniectomy remained open, and the patient met diagnostic criteria for minimal conscious state (MCS) as she consistently followed commands and could manipulate objects, but had no functional communication or object use. Testing using the Coma Recovery Scale Revised (CRS-R) (Giacino et al., 2004), showed a best total score of 14 (auditory 4, visual 3, motor 4, oro/motor 0, communication 1, and arousal 2). 8 months after injury, a right-sided cranioplasty restored the integrity of the entire skull. 10 months after injury, our second study was performed. At that time the patient demonstrated evidence of emergence from MCS based on recovery of functional object use, consistent communication, and improved attentional function (best CRS-R total score of 20 - auditory 4, visual 4, motor 6, oro/motor 2, communication 2, and arousal 2). In addition, physiological measurements using FDG-PET and resting state fMRI across the two visits showed marked changes (Voss et al., in press). A global increase in cerebral glucose utilization was seen, with regional increases in left mesial frontal cortex and the paramedian diencephalon. The resting state fMRI also changed in that the auditory resting-state network was identifiable only at the second visit. At the time of the studies, PS 2 was taking amantadine, modafinil, methylphenidate, levetiracetam (prophylactic only) and tizanidine (visit 2 only).

PS 3 was a 24-year-old woman who sustained a basilar artery thrombosis resulting in infarctions of the upper brainstem, bilateral central thalami, and left

medial temporal and occipital lobes as well as a resultant seizure disorder. Initial treatment consisted of seizure management and anticoagulation. The patient's clinical course was notable for a two-year period during which no evidence of command following had been noted and the presence of intermittent epileptic seizures, followed by discovery of an ability to communicate through eye movement. At the time of the first study reported here, 30 months after the infarct, the patient demonstrated intermittent evidence of communication consisting only of downward left eye movements as a "yes" response. At the second assessment, one year later, a brief period of control of an inward movement of the left eye to signal "no" was demonstrated; a more consistent use of this system had been established prior to the visit in the context of ongoing work with a speech therapist. At both visits, she had fluctuating arousal levels with periods of no behavioral response to commands. When she was responsive, she was able to move her left eye to command and showed evidence of orientation to self, location and situation, indicating a clinical status in the range of MCS to severe or moderate cognitive disability. A 2 to 3 Hz tremor of her jaw and face was present on both visits. During the second assessment, the patient's EEG showed frequent epileptiform activity and she had two clinical seizures. At the time of the studies PS 3 was taking amantadine and levetiracetam (visits 1 and 2) and modafinil and hyoscyamine (visit 2 only).

References

Giacino JT, Kalmar K, Whyte J. The JFK Coma Recovery Scale-Revised: Measurement characteristics and diagnostic utility. Arch Phys Med Rehabil 2004;85:2020-2029.

Teasdale G, Jennett B. Assessment of coma and impaired consciousness : A Practical Scale. Lancet 1974;304:81-84.

Voss HU, Heier LA, Schiff ND. Multimodal imaging of recovery of functional networks associated with reversal of paradoxical herniation after cranioplasty. Clin Imaging, In Press. doi:10.1016/j.clinimag.2010.07.008.

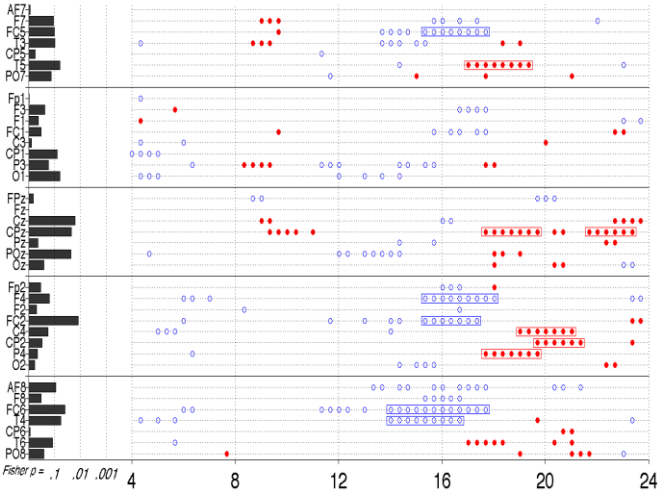
Supplementary Figure S1

HC 3 Motor Imagery

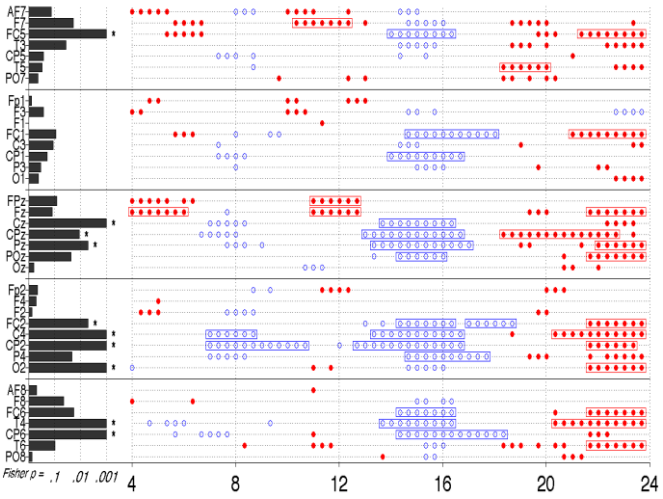
Swim > Rest

Rest > Swim

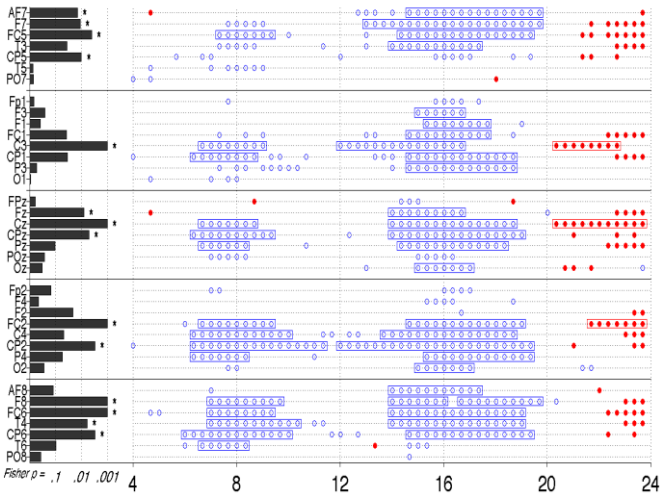
Run 1



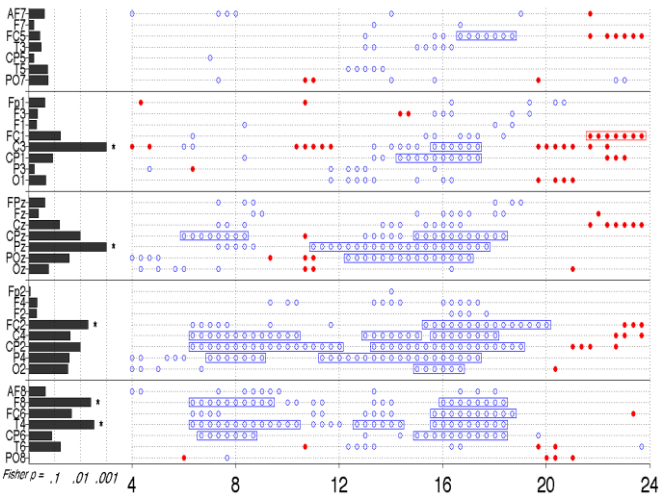
Run 2



Run 3



Run 4



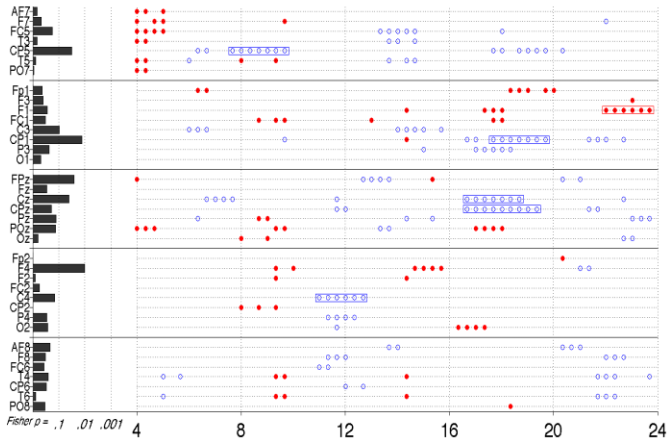
Supplementary Figure S2

HC 4 Motor Imagery

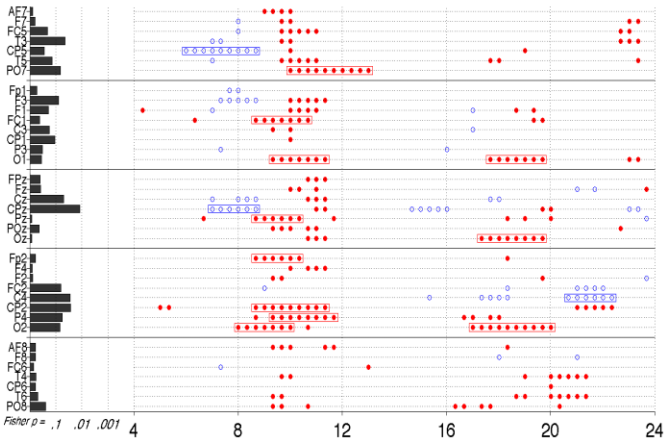
Swim > Rest

Rest > Swim

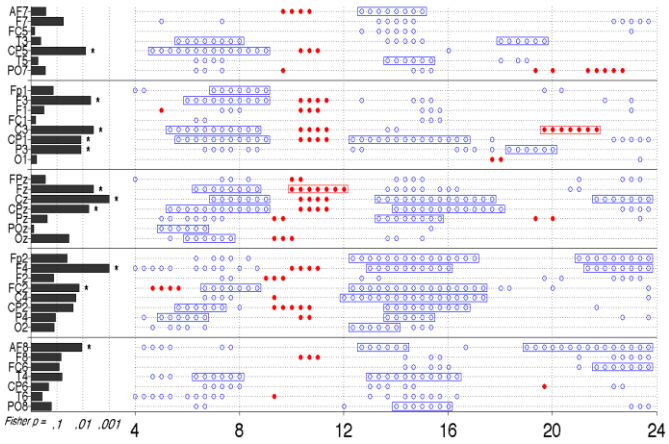
Run 1



Run 2



Run 3



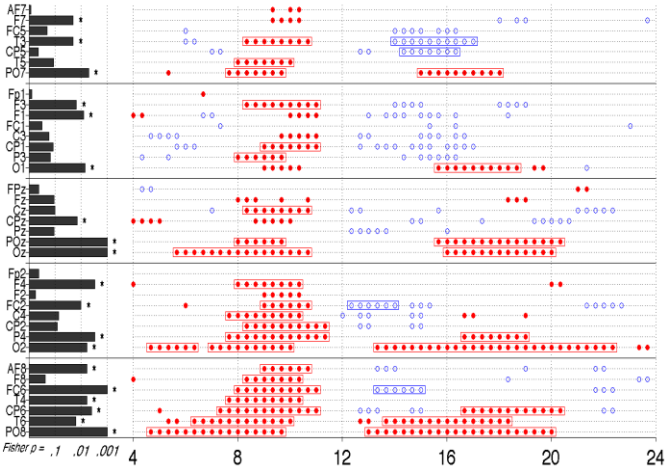
Supplementary Figure S3

HC 1 Navigation Imagery

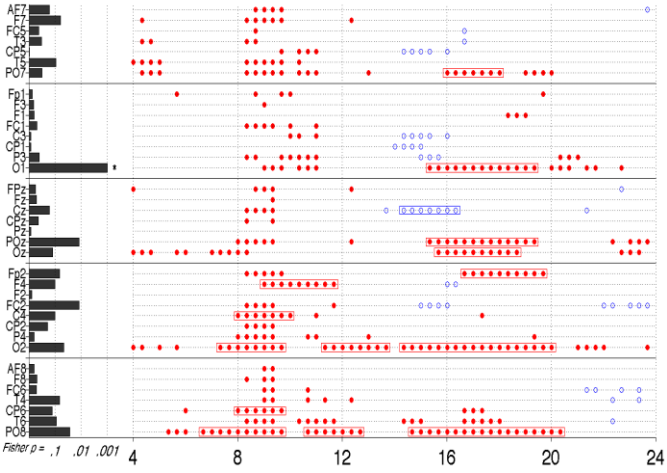
Nav > Rest

Rest > Nav

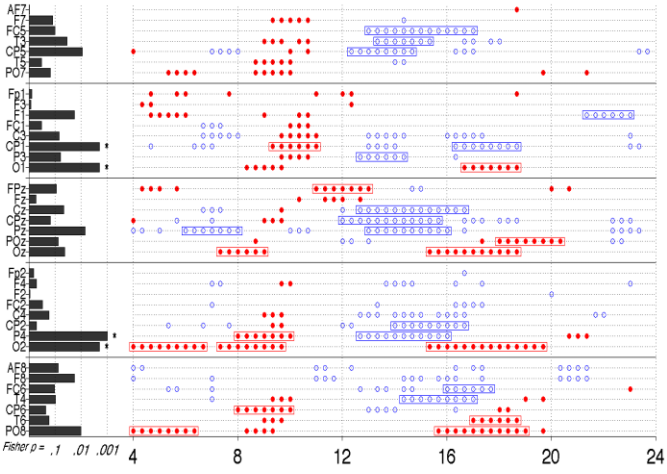
Run 1



Run 2



Run 3



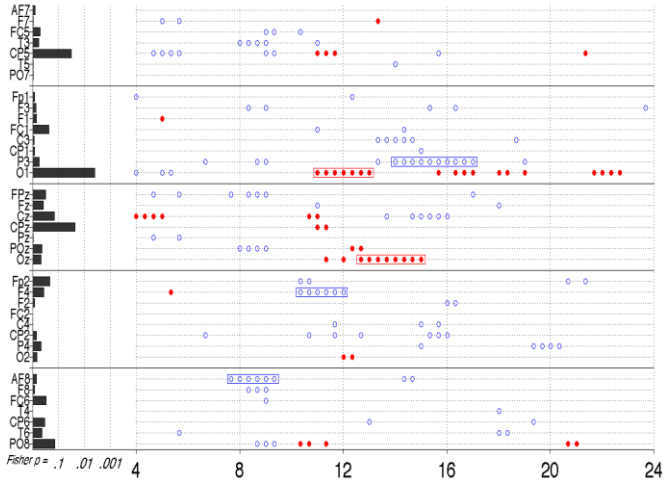
Supplementary Figure S4

HC 2 Navigation Imagery

Nav > Rest

Rest > Nav

Run 1



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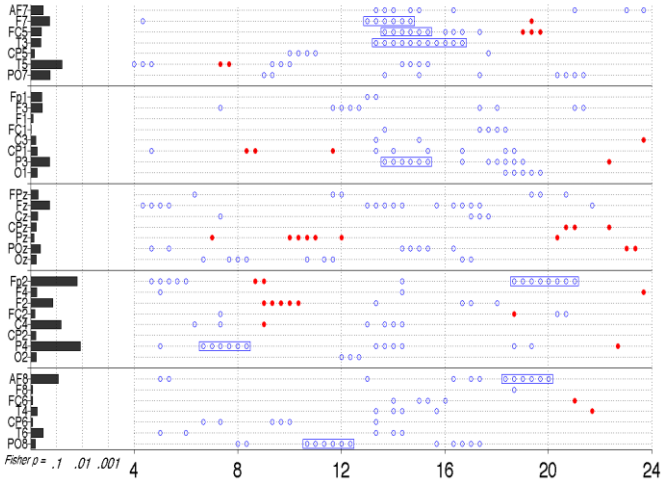

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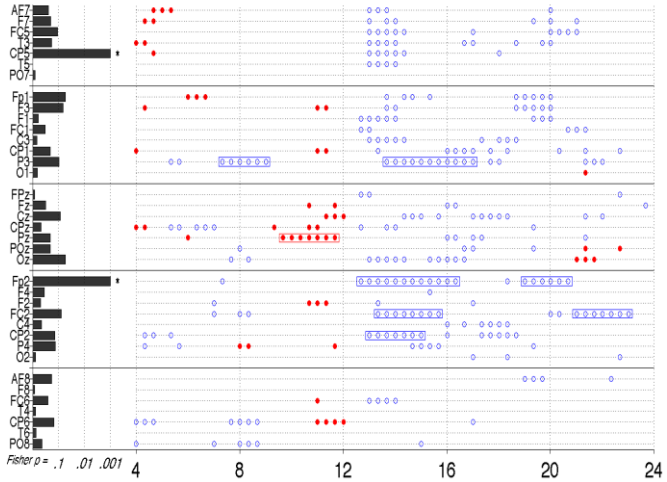

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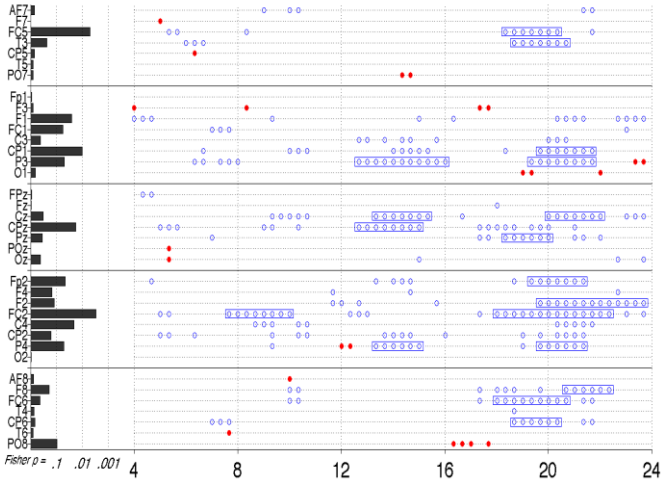


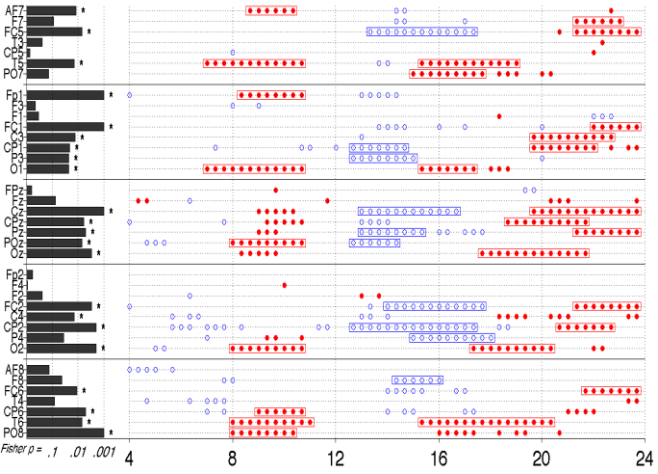
Supplementary Figure S5

HC 3 Navigation Imagery

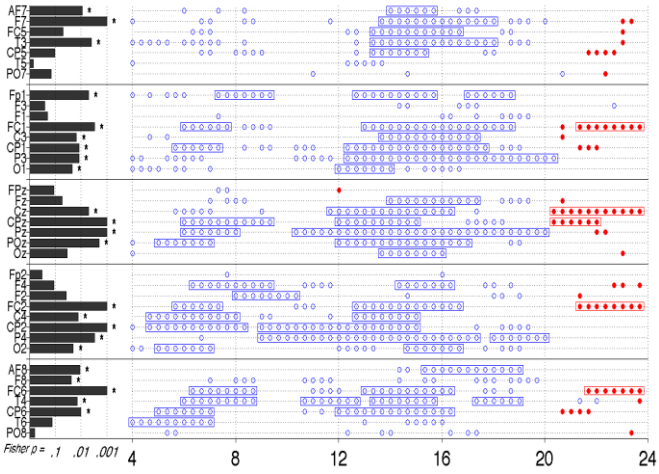
Nav > Rest

Rest > Nav

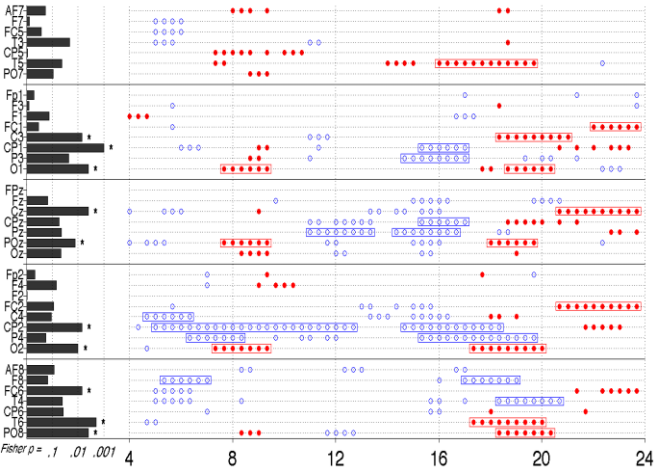
Run 1



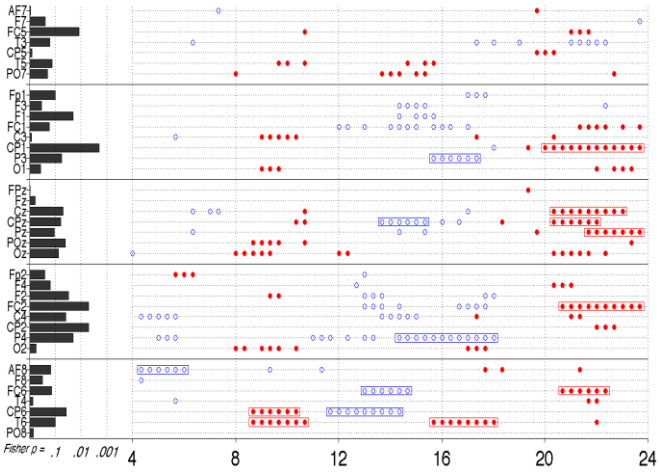
Run 2



Run 3



Run 4



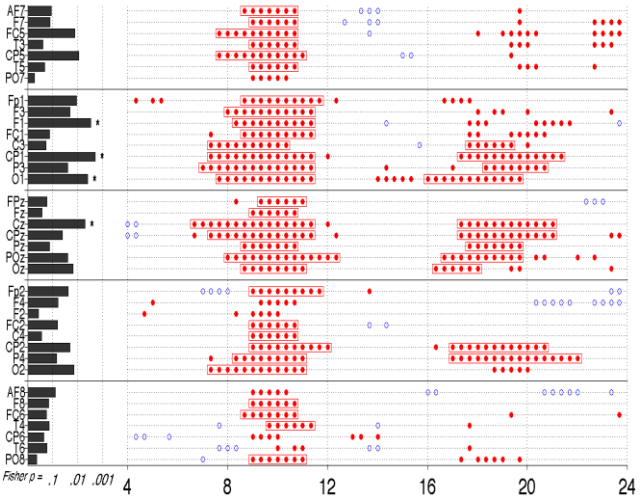
Supplementary Figure S6

HC 4 Navigation Imagery

Nav > Rest

Rest > Nav

Run 1



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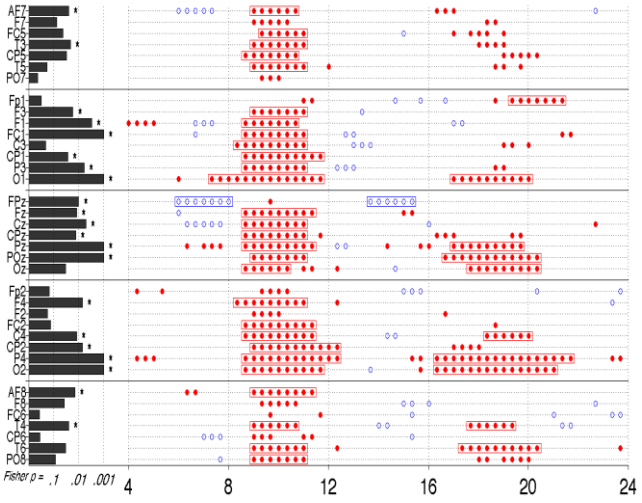
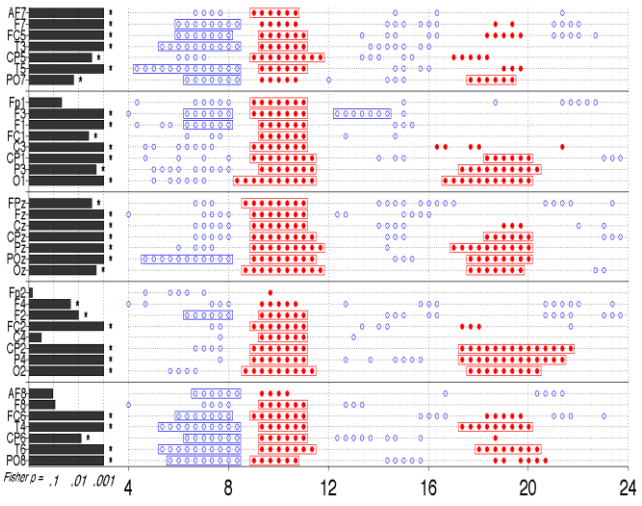


Run 3



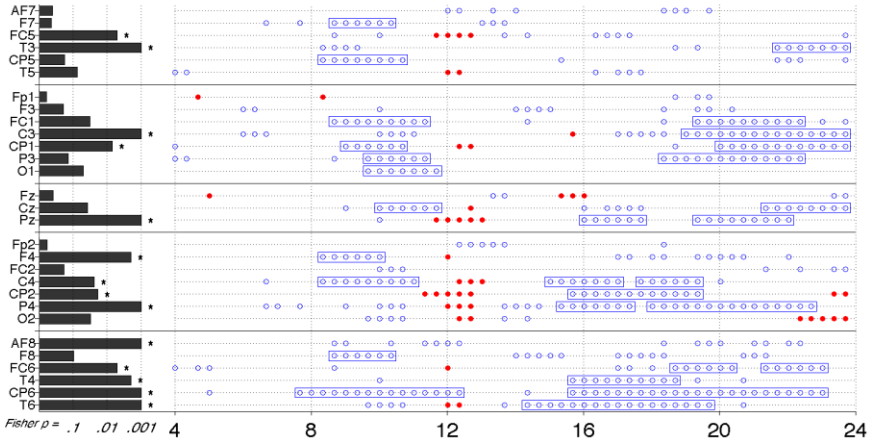
Supplementary Figure S7

HC 5 Navigation Imagery

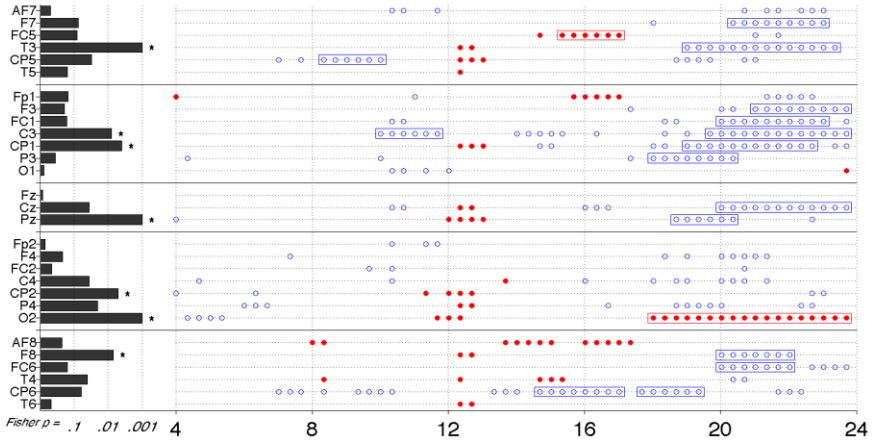
Nav > Rest

Rest > Nav

Run 1



Run 2



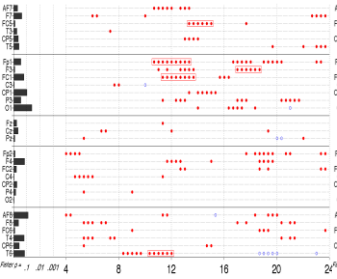
Supplementary Figure S8

PS 2 Visit 2 Motor Imagery

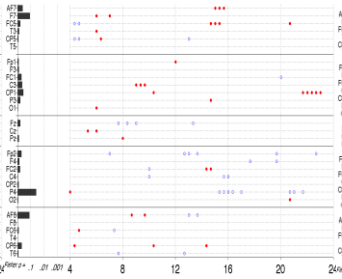
Swim > Rest

Rest > Swim

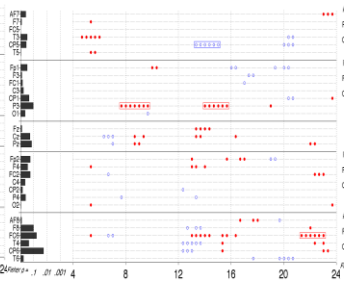
Run 1



Run 2



Run 3



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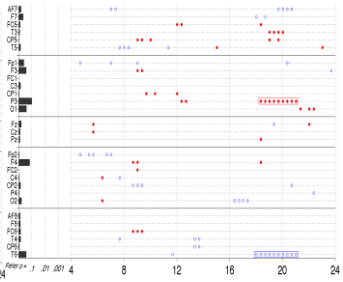
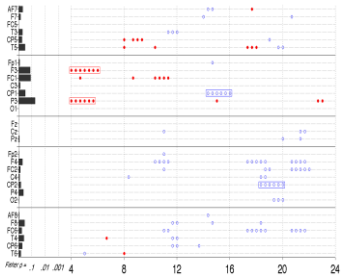
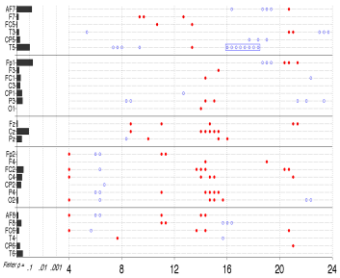


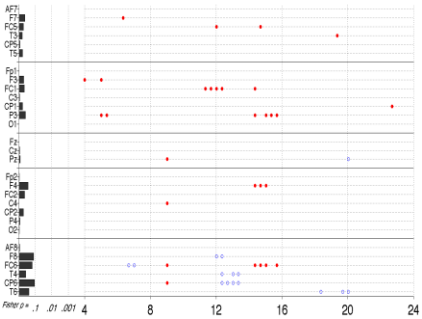
Run 5



Run 6



All Runs Combined



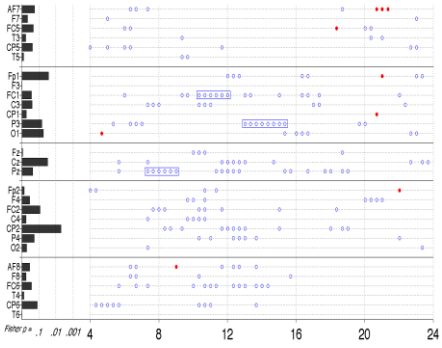
Supplementary Figure S9

PS 3 Visit 1 Navigation Imagery

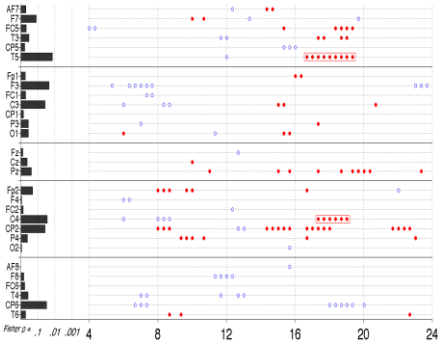
Nav > Rest

Rest > Nav

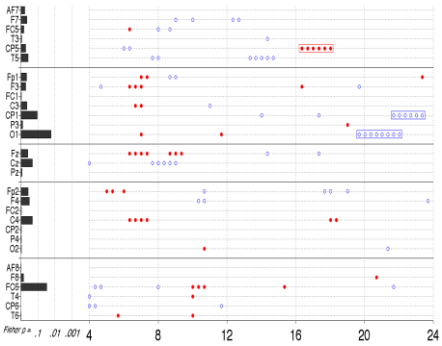
Run 1



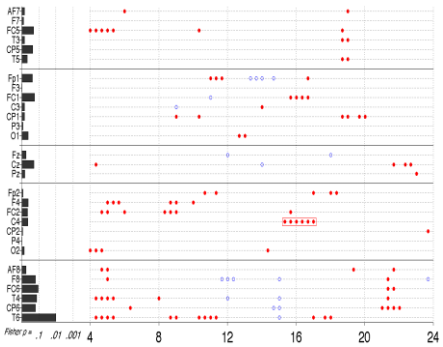
Run 2



Run 3



Run 4



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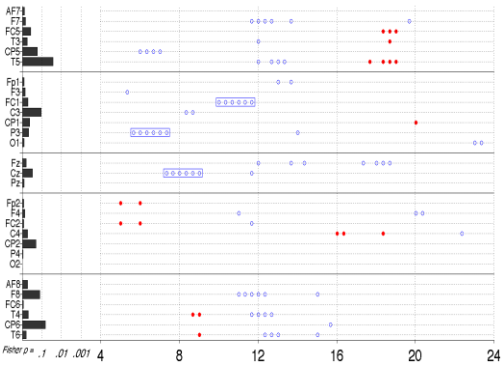


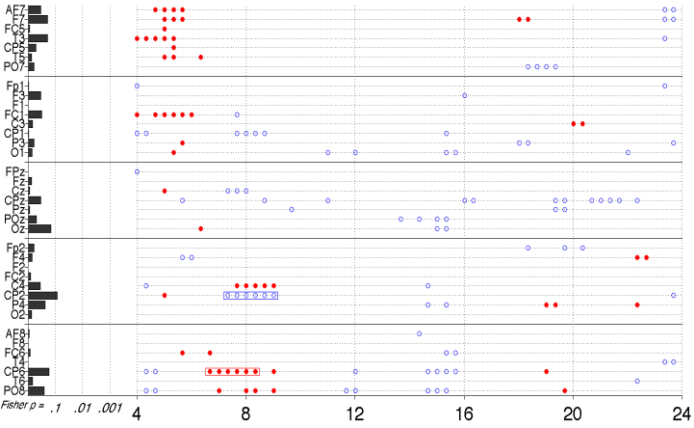
Supplementary Figure S10

PS 3 Visit 2 Motor Imagery

Swim > Rest

Rest > Swim

Run 1



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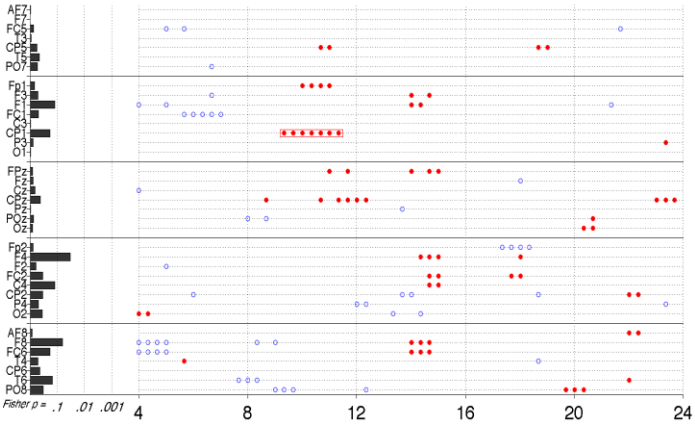
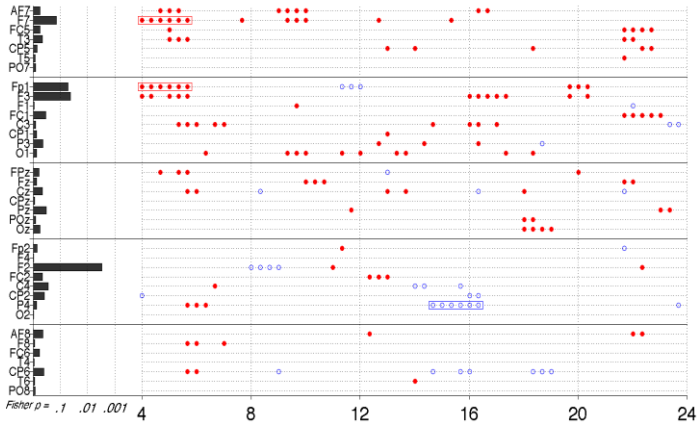


Run 3



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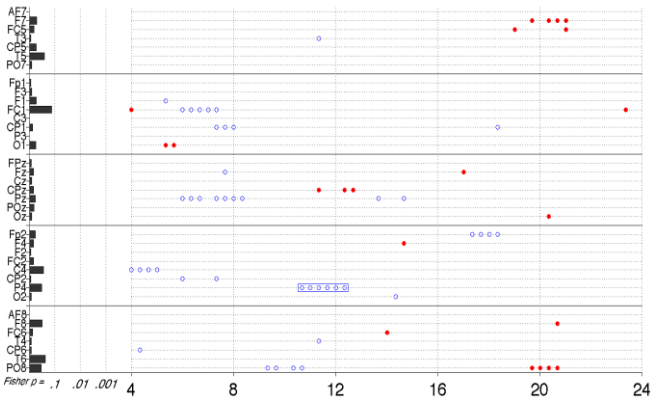
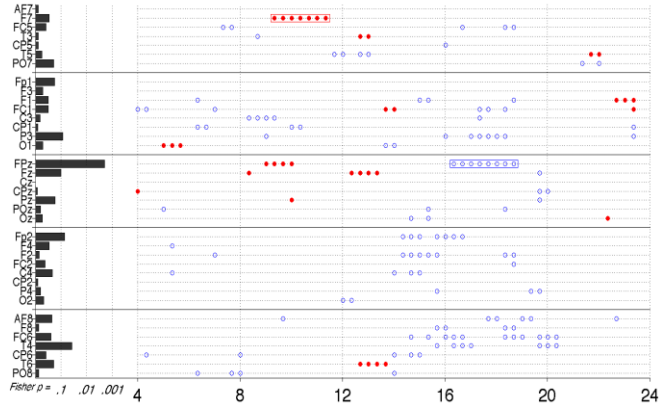


Supplementary Figure S11

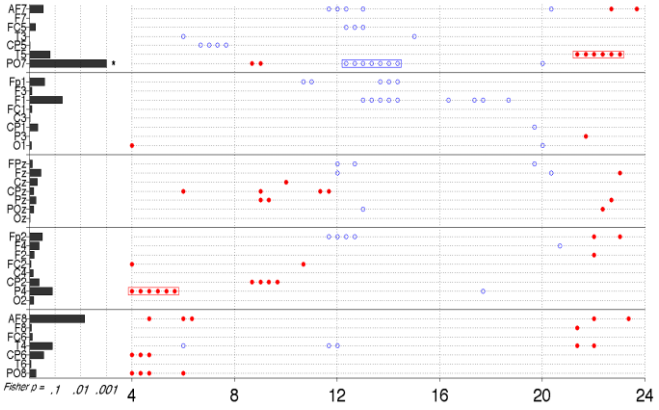
PS 3 Visit 2 – Navigation Imagery

Nav > Rest
Rest > Nav

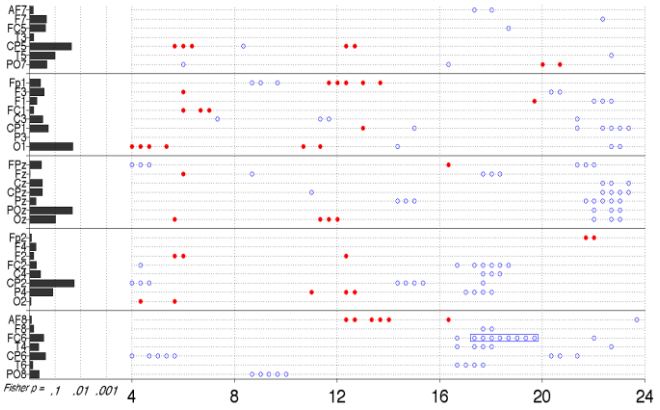
Run 1



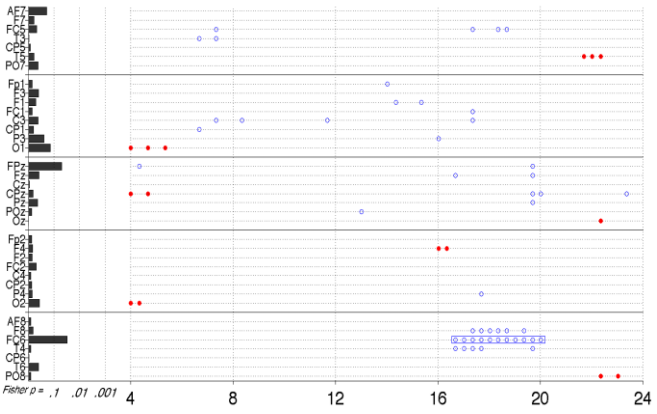
Run 2



Run 3



All runs combined



Supplementary Table S1

Subject	Task	Run	Snippets Used (max 48)	ICA Components Rejected	Percentage Variance Removed
HC1	Motor	1	48	10	32
		2	48	9	32
		3	48	7	32
	Nav	1	48	13	44
		2	48	15	46
		3	48	13	56
HC2	Motor	1	48	8	48
		2	48	15	67
		3	48	17	88
		4	48	17	86
	Nav	1	48	21	89
		2	48	20	83
		3	48	19	85
		4	48	19	85
HC3	Motor	1	48	5	21
		2	48	9	36
		3	48	10	30
		4	48	9	25
	Nav	1	48	9	36
		2	48	11	29
		3	48	9	25
		4	48	5	24
HC4	Motor	1	48	12	61
		2	48	12	48
		3	48	12	19
	Nav	1	48	14	32
		2	48	12	41
		3	48	14	30
HC5	Nav	1	48	2	24
		2	48	6	57
PS1	Motor	1	45	17	46
		2	30	16	56
PS2 (visit1)	Motor	1	48	20	91
		2	48	16	83
		3	48	7	84
PS2 (visit2)	Motor	1	48	11	93
		2	48	18	95
		3	48	11	82
		4	48	12	85
		5	48	11	78
		6	48	10	81
PS3 (visit1)	Motor	1	48	7	25
		2	48	8	24
		3	48	5	23
		4	48	5	23
	Nav	1	48	10	37
		2	48	5	22
		3	48	7	29
		4	48	6	20
PS3 (visit2)	Motor	1	48	18	66
		2	48	14	19
		3	48	9	18
	Nav	1	48	17	52
		2	48	14	24
		3	27	12	14