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Consciousness-Motor Dissociation in Chronic TBI: Zolpidem Effect in Kernohan's Notch Syndrome

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Background

Zolpidem can paradoxically restore consciousness in some patients with disorders of consciousness (DoC). However, behavioral assessment can be challenging when severe structural motor pathway damage coexists. We report a unique case of a chronic traumatic brain injury (TBI) patient with Kernohan's notch syndrome, where Zolpidem induced a significant "consciousness awakening" despite persistent quadriplegia.

Case report

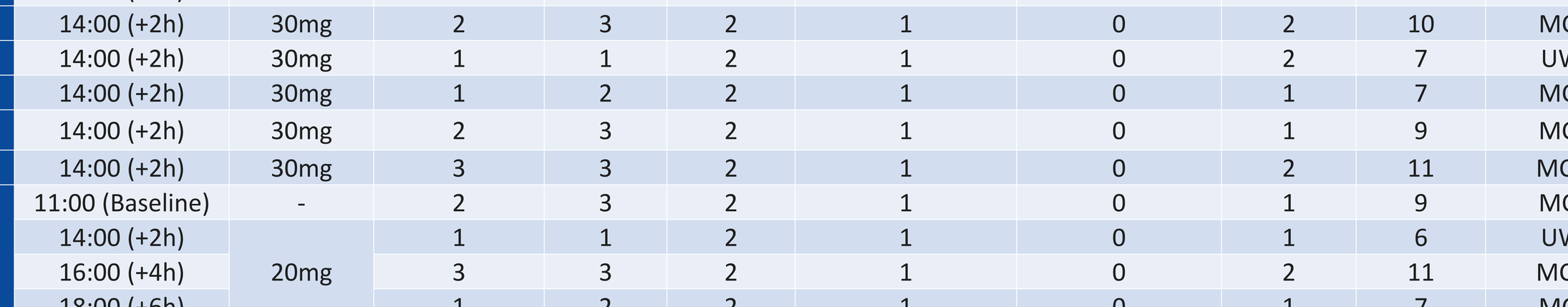
A 68-year-old female in an Unresponsive Wakefulness Syndrome (UWS) for 8 months following a traumatic subdural hematoma was admitted for intensive rehabilitation. Brain MRI revealed extensive encephalomalacia in the bilateral frontal lobes and ipsilateral cerebral peduncle compression (Kernohan's notch syndrome), explaining her persistent quadriplegia (MMT grade 1) with Wallerian degeneration of the midbrain and pons. To exclude confounding effects, concurrent neuropharmacological treatments, including amantadine and donepezil, were maintained at stable dosages for at least 4 weeks prior to evaluation. Systematic Zolpidem titration (10 mg to 30 mg) was performed. At the optimal dose of 20 mg, her JFK CRS-R score dramatically improved from 7 (UWS) to 15 (EMCS). Notably, she achieved consistent auditory command following (A4), functional communication (C2) and sustained attention (Ar3) at 4-6 hours post-dose, reflecting a delayed peak response compared to typical pharmacokinetics.

Slow waves were recorded on EEG before medication ('Zolpidem-off'), and the reversal of slow wave to beta range fast activity ,which is dominant waveform in alert and attentive individuals, was detected after medication ('Zolpidem-on') on right temporal lobe. FDG-PET imaging during the 'Zolpidem ON' state showed a qualitative increase in glucose metabolism (shifting from blue to green uptake) within right parahippocampal gyrus, amygdala and entorhinal cortex compared to the 'Zolpidem OFF' state. Furthermore, VFSS demonstrated an improvement in swallowing safety; the PAS improved from 8 to 1 for 12% semisolid and from 8 to 3 for small liquid. During peak arousal, the patient exhibited intentional spitting of contrast media, indicating the emergence of cognitive rejection.

Table 1. Time-dependent response of the Zolpidem effect

Date	Time Point	Dosage	Auditory	Visual	Motor	Oromotor/Verbal	Communication	Arousal	Total Score	Diagnosis
Feb 13	11:00 (Baseline)	-	1	2	0	1	0	2	6	UWS
	14:00 (+2h)	20mg	2	2	2	1	0	1	8	MCS-
	16:00 (+4h)		2	3	2	2	0	2	11	MCS-
	18:00 (+6h)		2	3	0	1	0	1	7	MCS-
Feb 14	14:00 (+2h)	30mg	2	3	2	1	0	2	10	MCS-
Feb 15	14:00 (+2h)	30mg	1	1	2	1	0	2	7	UWS
Feb 16	14:00 (+2h)	30mg	1	2	2	1	0	1	7	MCS-
Feb 17	14:00 (+2h)	30mg	2	3	2	1	0	1	9	MCS-
Feb 18	14:00 (+2h)	30mg	3	3	2	1	0	2	11	MCS+
Feb 19	11:00 (Baseline)	-	2	3	2	1	0	1	9	MCS-
	14:00 (+2h)	20mg	1	1	2	1	0	1	6	UWS
	16:00 (+4h)		3	3	2	1	0	2	11	MCS+
	18:00 (+6h)		1	2	2	1	0	1	7	MCS-
Feb 23	11:00 (Baseline)	-	2	3	2	1	0	1	9	MCS-
	14:00 (+2h)	20mg	3	3	2	1	0	2	11	MCS-
	16:00 (+4h)		4	3	2	1	0	3	13	MCS+
	18:00 (+6h)		4	3	2	1	0	3	13	MCS+
Mar 19	11:00 (Baseline)	20mg	4	3	2	1	1	3	14	MCS+
	16:00 (+4h)		4	3	2	1	2	3	15	EMCS

UWS, Unresponsive Wakefulness Syndrome; MCS-, Minimally Conscious State minus; MCS, Minimally Conscious State; MCS+, Minimally Conscious State plus; EMCS, Emergence from MCS



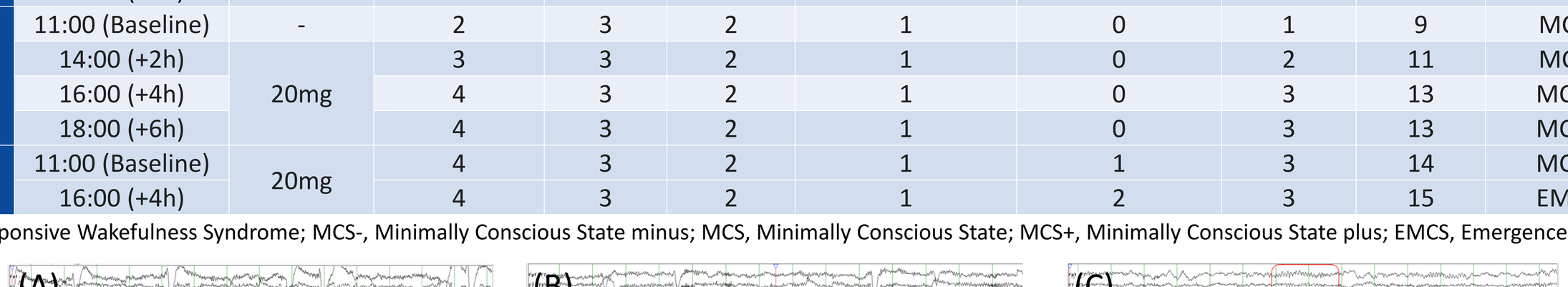


Fig. The electroencephalography show the reversal of slow wave to beta range fast activity after medication (A) Zolpidem-on for 2hrs, (B) Zolpidem-on for 4 hrs, and slow wave before medication (C) Zolpidem-off. Brain metabolism images in zolpidem on and off states (D) Right parahippocampal gyrus, (E) Right amygdala and right entorhinal cortex

Conclusion

This case highlights a "bell-shaped" dose-response curve of Zolpidem, where 20 mg was superior to 30 mg due to the latter's overriding sedative effect. The dissociation between high auditory/visual scores and persistent motor deficits emphasizes that behavioral motor output alone may underestimate the level of consciousness in patients with brainstem pathway disruption. Comprehensive evaluation including FDG-PET should be considered to identify the full therapeutic potential of Zolpidem in complex DoC cases.