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Research Report

Cognitive dysfunction might be improved in association with recovered neuronal viability after intracranial meningioma resection

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ABSTRACT

Intracranial meningiomas are the most common types of neoplasms that cause mental disorders. Although higher brain function can be restored and even improved in some patients after tumor resection, the mechanisms remain unclear. We investigated changes in the brains of patients after resection of an intracranial meningioma using ^{123}I-Iomazenil (IMZ)-single photon emission computed tomography (SPECT).

Ten patients underwent IMZ-SPECT within 4 weeks before and 3 months after intracranial meningioma resection. Changes in IMZ accumulation in brain parenchyma were assessed as ratios of counts in the lesion-to-contralateral hemisphere (L/C ratios).

Mean Mini-Mental State Examination scores before and after resection of 19.9±11.4 vs. 26.5±3.8, respectively ($p=0.03$) indicated that the cognitive function of these patients was significantly improved after tumor resection. The average L/C ratios calculated from image counts of IMZ were 0.92±0.05 and 0.98±0.02 before and after surgery, respectively. The L/C ratio of IMZ accumulation was significantly decreased after tumor resection ($p=0.0003$). In contrast, regional cerebral blood flow calculated from ^{123}I-Iodoamphetamine-SPECT images did not significantly differ after tumor resection.

The recovered binding potential of IMZ in brain parenchyma surrounding the tumor bulk after resection indicates that the viability of central benzodiazepine receptors was reversibly depressed and recoverable after release from compression by the tumor. The recovered neuronal viability revealed by IMZ-SPECT might be responsible for the improved cognitive function after intracranial meningioma resection.

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1. Introduction

About 90% of meningiomas that primarily arise from the meningeal coverings are benign and correspond to World Health Organization (WHO) grade I (Louis et al., 2000). However, meningiomas slowly enlarge and sometimes exert firm pressure on the gray matter of the surrounding cortices. They are also the most frequent causative neoplasms of mental disorders (Andy et al., 1981; Carlsson et al., 2010; Dijikstra et al., 2009; Feder et al., 1989; Gazzeri et al., 2008; Goto et al., 2003; Krupp et al., 2009; Lampl et al., 1995; Leimkuhler and Mesulam, 1985; Maurice-Williams and Dunwoody, 1988; Selecki, 1965; Simoca et al., 1994; Tucha et al., 2000, 2003). Although cognitive disturbances including aphasia, confusion and disorientation arise in 25–62% of patients with intracranial meningiomas (Feder et al., 1989; Simoca et al., 1994), higher brain function has been restored after tumor resection in some of them (Carlsson et al., 2010; Gazzeri et al., 2008; Goto et al., 2003; Tucha et al., 2003). However, the mechanisms responsible for retrieved neurocognitive ability remain unclear. The effects of meningioma lateralization, anatomical localization, lesion size, edema and brain compression on cognition have been analyzed (Dijikstra et al., 2009; Krupp et al., 2009; Lampl et al., 1995; Tucha et al., 2003). However, other than these anatomically-related investigations, the pathophysiological mechanisms of impaired neurocognitive function have not been specifically examined in detail. To verify preserved cortical neuron viability in the peri-tumor region is considered vital to understanding the pathogenesis of cognitive dysfunction that may remain unaltered or significantly improved after tumor resection. Here, we used ^{123}I-Iomazenil (IMZ)-single photon emission computed tomography (SPECT) to assess the viability of cerebral cortical neurons in the brains of patients before and after the surgical resection of supratentorial meningiomas.

The radioligand IMZ specifically binds to central benzodiazepine receptors (CBZR) and it was developed as a tracer for SPECT. Central benzodiazepine receptors are postsynaptic membrane receptor ionophore complexes that harbor gamma-aminobutyric acid (GABA) receptors and they exist at variable densities in neuronal membranes. The binding potentials of CBZR ligands such as flumazenil (FMZ) and IMZ are ideal markers of neuronal integrity and they can help to detect neuronal loss after ischemic stroke (Hatazawa et al., 1995; Heiss et al., 1998; Rudolf et al., 2000). Since IMZ images reflect receptor density and imply the distribution and existence of cortical neurons, the recently reported reduction in the binding potentials of IMZ has been associated with cognitive impairment in patients with ischemic stroke, Alzheimer's disease, and other psychiatric diseases (Ball et al., 1998; Chida et al., 2009; Fukuichi et al., 1997; Hanyu et al., 2012; Pappata et al., 2010; Prohovnik, 1998; Varrone et al., 1999; Yamashita et al., 2012).

A reduction in the binding potentials of radioligand for CBZR has long been considered irreversible because IMZ and FMZ accumulation has never recovered during the chronic stage of ischemic stroke (Hatazawa et al., 1995; Heiss et al., 1997, 1998, 2000; Rudolf et al., 2000). However, we recently discovered that IMZ accumulation can recover after traumatic brain injury (Koizumi et al., 2010), and considered that the binding affinity of CBZR was reversibly restrained during the acute stage of such injury and recovered during the chronic stage when cerebral metabolism normalized. We speculated that if IMZ SPECT could visualize changes in CBZR distribution at peri-tumor regions in the cortex before and after tumor resection, then images of receptor distribution might serve as crucially important evidence of recovered neuronal viability being responsible for improving cognitive deficits.

Correlations between regional cerebral blood flow (rCBF) and brain edema around tumor bulk are essentially unknown. Furthermore, rCBF assessment in association with changes in IMZ binding potential is extremely important to identify whether or not blood flow is preserved so that the CBZR tracer can be delivered to compressed cortices around the tumor bulk.

The present study uses IMZ SPECT and ^{123}I-iodoamphetamine (IMP) SPECT to evaluate the viability of neurons and to measure rCBF in the cortices of areas surrounding supratentorial meningiomas before and after resection in association with improved cognitive function. We subsequently identified a notable phenomenon, which we describe herein along with a review of the literature.

2. Results

Karnofsky Performance status (KPS) is a fundamental index that classifies cancer patients according to functional impairment scores ranging from 0 to 100% (Schag et al., 1984). We also statistically analyzed the KPS scores of all patients within 4 weeks before and 3 months after tumor resection (Table 1) and

Table 1 – Clinical features of the patients.

Patient no.	Age (years)	Sex	Tumor location	Tumor volume (ml)	Karnofski performance status (%)		Mini-Mental State Examination (MMSE)	
					Presurgery	Postsurgery	Presurgery	Postsurgery
1	76	F	Lt. parasagittal	182	40	70	29	30
2	55	F	Lt. parasagittal	35.1	90	100	20	29
3	72	M	Rt. convexity	107	60	90	29	30
4	48	F	Lt. parasagittal	32.2	80	100	30	30
5	51	F	Lt. parasagittal	49.5	100	100	30	30
6	63	F	Lt. parasagittal	36.4	90	100	24	25
7	87	M	Rt. convexity	96.4	40	80	5	21
8	74	F	Rt. convexity	150.1	20	60	5	21
9	79	M	Lt. convexity	119.3	40	90	2	23
10	76	M	Rt. parasagittal	82.7	70	90	25	26