るのではないかと推定している[11]．

convulsive syncope におけるけいれんにおいても，脳局所の機能異常の存在が想定されているが，これまでその詳細はわかっていない．convulsive syncope の際に，tonic spasm 様の不随意運動を呈することや，除脳硬直や除皮質硬直様の姿位をとることがある．これは，虚血により影響を受けやすい大脳皮質が機能低下をおこして脳幹への抑制が解除された結果，脳幹の活動が相対的に高まることで症状が発現するのではないかと Gastaut らは推察している[2]．一方で，Riley らは右半球皮質の陳旧性脳梗塞病変を有する患者で，起立性低血圧にともなって左上肢の rhythmical contraction を呈した症例を報告している[18]．この症例では，患者を臥位から座位にさせた後に，症状が出現するとともに，脳波上では右半球優位の全般性の徐波が出現した．そのため，虚血に対して脆弱性のある右半球の皮質由来のけいれんが，起立性低血圧により誘発されたのではないかと彼らは推測している．

本症例においては，けいれん様不随意運動発現時に，左基底核および両側前頭葉，右小脳半球の相対的血流低下がおこっていることが脳血流 SPECT で示された．今回の解析方法では血流の絶対値を評価することはできないため，発作時に脳全体の血流低下がおこっていたばあいはこれを検出することはできない．しかし局所的カウントを全脳のカウントで標準化する解析方法であるため，全脳の血流が低下していたばあいは左基底核の血流低下は過小評価されることになるにもかかわらず，差分画像でこれらの部位の血流低下が検出されていることから，同部位の血流低下の程度は検出されたよりも大きいと考えられる．一方で，右基底核の血流低下は検出できなかった可能性がある．両側前頭葉の血流低下については，起立性低血圧や両側内頸動脈狭窄を有する患者では，立位負荷によって不随意運動発現の有無にかかわりなく生じうることが報告されている[19]．一方で，本症例ではとくに左の大脳基底核(尾状核)の血流低下が顕著であることが注目され，右上肢優位のけいれん様不随意運動との関連が示唆される．尾状核の虚血性病変によって chorea や dystonia，tremor などの不随意運動が生ずることがある[20][21]．本症例においては頭部 MRI および CT 血管撮影では，主幹動脈の著明な狭窄はみとめられなかったが，基底核を灌流する穿通枝動脈の狭窄の存在は否定できない．また，右小脳半球の血流低下については，内包前脚付近の虚血にともなって生じた crossed cerebellar diaschisis (CCD：対側小脳半球の血流低下) の可能性が考えられた[22]．

convulsive syncope では，発作時に様々な運動症状を呈する．その中で，本症例のようなけいれん様の不随意運動を呈するものの中には，大脳皮質よりもむしろ基底核の低灌流にともなう機能不全が不随意運動の発生に関与しているものがあると推定される．今後，更なる症例の蓄積が望まれる．

文　献

1) Sheldon RS, Koshman ML, Murphy WF. Electroencephalographic findings during presyncope and syncope induced by tilt table testing. Can J Cardiol 1998;14:811-816.
2) Gastaut H, Fischer-Williams M. Electro-encephalographic study of syncope; its differentiation from epilepsy. Lancet 1957;273:1018-1025.
3) Ozkara C, Metin B, Kucukoglu S. Convulsive syncope: a condition to be differentiated from epilepsy. Epileptic Disord 2009;11:315-319.
4) Yanagihara T, Piepgras DG, Klass DW. Repetitive involuntary movement associated with episodic cerebral ischemia. Ann Neurol 1985;18:244-250.
5) Tatemichi TK, Young WL, Prohovnik I, et al. Perfusion insufficiency in limb-shaking transient ischemic attaks. Stroke 1990;21:341-347.
6) Firlik AD, Firlik KS, Yonas H. Physiological diagnosis and surgical treatment of recurrent limb shaking: Case Report. Neurosurgery 1996;39:607-611.
7) Klempen NL, Janardhan V, Schwartz RB, et al. Shaking limb transient ischemic attacks: unusual presentation of carotid artery occlusive disease: report of two cases. Neurosurgery 2002;51:483-487.
8) 和田祐子，喜多也寸志，山本　徹．血行力学的一過性脳虚血発作により limb shaking と変形視を反復した本態性起立性低血圧の一例．臨床神経 2000;40:582-585.
9) Han SW, Kim SH, Kim JK, et al. Hemodynamic changes in limb shaking TIA associcated with anterior cerebral artery stenosis. Neurology 2004;63:1519-1521.
10) Khan A, Beletsky V, Kelley R, et al. Orthostatic-mediated hypoperfusion in limb-shaking transient ischemic attack. J Neuroimaging 1999;9:43-44.
11) Im SH, Oh CW, Kwon OK, et al. Involuntary movement induced by cerebral ischemia: pathogenesis and surgical outcome. J Neurosurg 2004;100:877-882.
12) Kim HY, Chung CS, Lee J, et al. Hyperventilation-induced limb shaking TIA in moyamoya disease. Neurology 2003;60:137-139.
13) Kim YO, Kim TS, Woo YJ, et al. Moyamoya disease-induced hemichorea corrected by indirect bypass surgery. Pediatrics International 2006;48:504-506.
14) Hashikawa K, Matsumoto M, Moriwaki H, et al. Split dose iodine-123-IMP SPECT: sequential quantitative regional cerebral blood flow change with pharmacological intervention. J Nucl Med 1994;35:1226-1233.
15) Grubb BP, Gerard G, Roush K, et al. Differentiation of convulsive syncope and epilepsy with head-up tilt testing. Ann Intern Med 1991;115:871-876.
16) 平賀旗夫，青木恭規，児玉南海雄．Moyamoya 病の脳波—その診断的価値と類型化について—．臨床脳波 1980;22:513-525.
17) 唐澤　淳，菊池晴彦，高橋伸明ら．小児 "もやもや病" の脳

波. 臨床脳波 1980;22:527-536.
18) Riley TL, Friedman JM. Stroke, Orthostatic Hypotention, and focal seizures. JAMA 1981;245:1243-1244.
19) Hayashida K, Nishiooeda Y, Hirose Y, et al. Maladaptation of vascular response in frontal area of patients with orthostatic hypotension. J Nucl Med 1996;37:1-4.
20) Saris S. Chorea caused by caudate infarction. Arch Neurol 1983;40:590-591.
21) Bhatia KP, Marsden CD. The behavioral and motor consequences of focal lesions of the basal ganglia in man. Brain 1994;117:859-876.
22) Liu Y, Karonen JO, Nuutinen J, et al. Crossed cerebellar diaschisis in acute ischemic stroke: a study with serial SPECT and MRI. J Cereb Blood Flow Metab 2007;27:1724-1732.

Abstract

Convulsive syncope associated with transient hemodynamic ischemia in the basal ganglia

Takashi Murahara, M.D.[1][4], Shigetoshi Takaya, M.D.[2][3], Daisuke Yamaguchi, M.D.[1], Tomohiro Tanaka, M.D.[1], Hidenao Fukuyama, M.D.[2], Akio Ikeda, M.D.[1] and Ryosuke Takahashi, M.D.[1]
[1]Department of Neurology, Graduate School of Medicine, Kyoto University
[2]Human Brain Research Center, Graduate School of Medicine, Kyoto University
[3]Radioisotope Research Center, Kyoto University
[4]Department of System Neuroscience, School of Medicine, Sapporo Medical University

The pathophysiology of convulsive movements in patients with convulsive syncope remains unclear. Here, we report a patient with convulsive syncope whose convulsive movements seemed to be associated with transient hemodynamic ischemia in the basal ganglia. A 74-year-old man had 1-year history of orthostatic hypotension and transient clonic jerks in the limbs and trunk, predominantly in the right upper limb. His convulsive movements were evoked approximately 1 minute after sitting up or standing up from the supine position and lasted for several tens of seconds. He felt mild faint while the convulsive movements lasted, but he was oriented and could follow simple commands. He was diagnosed as pure autonomic failure. Video-electroencephalogram (EEG) recorded generalized slows without any epileptiform discharges when the symptoms appeared. Single-photon emission computed tomography (SPECT) was performed using split-dose method to evaluate the change in blood flow when the convulsive movements appeared. During symptoms, a significant decrease in blood flow was revealed in the anterior part of the left basal ganglia, bilateral frontal areas, and right cerebellar hemisphere. An alteration in the functional balance between the basal ganglia and the cerebral cortices may play a role in the generation of convulsive movements in patients with convulsive syncope.

(Clin Neurol 2011;51:338-344)

Key words: convulsive syncope, electroencephalography, SPECT, orthostatic hypotension

INTERNAL MEDICINE

□ ORIGINAL ARTICLE □

Reversible Alcohol-related Dementia: A Five-year Follow-up Study Using FDG-PET and Neuropsychological Tests

Tomohiko Asada[1], Shigetoshi Takaya[1,2], Yoshihiro Takayama[3], Hiroshi Yamauchi[1], Kazuo Hashikawa[1,4] and Hidenao Fukuyama[1]

Abstract

Objective As the pathophysiology of alcohol-related dementia (ARD) is unclear, we examined a patient with reversible ARD using neuropsychological tests and ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET).

Methods Design: A five-year follow-up case study with neuropsychological tests and FDG-PET. Setting: Kyoto University Hospital.

Patients A 42-year-old patient who was unable to perform his office duties because of slowly progressive amnesia with executive dysfunction.

Results The initial evaluation with neuropsychological tests showed severe verbal memory disturbance. The patient did not discuss his excessive alcohol consumption in the initial history-taking session and thiamine deficiency was absent; therefore, early-stage Alzheimer's disease was suspected. Later, the patient revealed prior excessive alcohol intake and his cognitive function improved markedly after a period of abstinence. Retrospective analysis of initial FDG-PET images using a voxel-wise statistical method revealed glucose hypometabolism in the diencephalon and basal forebrain. Follow-up for 5 years after the initial evaluation showed improved cognitive function and recovery of glucose metabolism in the two brain regions.

Conclusion Hypofunction in the diencephalon and basal forebrain was associated with cognitive decline in our patient. This case may provide evidence for the etiopathic brain regions in reversible type ARD.

Key words: alchohol related dementia, Wernicke-Korsakoff syndrome, FDG-PET, Alzheimer disease, diencephalon, basal forebrain

(Inter Med 49: 283-287, 2010)
(DOI: 10.2169/internalmedicine.49.2662)

Introduction

The Wernicke-Korsakoff syndrome (WKS) is a representative alcohol-induced memory disturbance characterized by neuropathological changes in the diencephalon, including the anterior part of the thalamus, and the mammillary body caused by thiamine deficiency (1). The most characteristic neuropsychological feature of WKS is marked memory deficits, while the other intellectual abilities are relatively preserved (2, 3). An ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) study of WKS showed regional glucose hypometabolism in the diencephalic grey matter, which is consistent with the underlying neuropathology. Glucose hypometabolism was also found in the medial temporal lobe and retrosplenium, which is interpreted as secondary metabolic effects within the diencephalic-limbic memory circuits (4).

Alcohol-related dementia (ARD) has been broadly defined as alcohol-induced dementia in the Diagnostic and Statistical Manual of Mental Disorders IV- Text Revision (DSM-IV-TR). ARD has been reported as the organic brain syndrome induced by alcohol abuse, which results in severe cognitive impairment, including executive dysfunction and lack of

[1]Human Brain Research Center, Kyoto University Graduate School of Medicine, Kyoto, [2]Radioisotope Research Center, Kyoto University, Kyoto, [3]Department of Speech Physiology, Graduate School of Medicine, University of Tokyo, Tokyo and [4]National Hospital Organization, Osaka Minami Medical Center, Kawachinagano
Received for publication July 7, 2009; Accepted for publication October 8, 2009
Correspondence to Dr. Hidenao Fukuyama, fukuyama@kuhp.kyoto-u.ac.jp

Table 1. Results of Neuropsychological Assessments

Battery	On admission	3 weeks after admission	5 years after discharge
Mini-Mental State Examination	30 (full marks)	ND	30
WAIS-R			
VIQ	100	ND	130
PIQ	107	ND	137
FIQ	104	ND	137
Geriatric Depression Scale	15 (full marks)	ND	0
Miyake's Verbal Memory Test			
Associated paired-word test	9–10–10	ND	10–10–10
Nonassociated paired-word test	1–4–4	6–7–6	8–10–10

WAIS-R: Wechsler Adult Intelligence Scale-Revised ; VIQ: verbal intelligence quotient; PIQ: performance intelligence quotient; FIQ: full-scale intelligence quotient; ND: not done

emotional control, in addition to memory disturbance (5). Although the pathophysiology of WKS has been relatively well studied, the neural basis of ARD remains unclear. Two concepts have been proposed for ARD: 1) ARD is a variant of WKS and is associated with thiamine deficiency-induced dysfunction in the diencephalon (6) and 2) ARD originates from the disturbance impairment of the cholinergic system, including projection fibers from the nucleus basalis of Meynert or the dorsal brainstem (7-12). Functional neuroimaging techniques such as PET have been expected to elucidate the neural substrate of ARD (13).

Here, we describe a series of neuropsychological and FDG-PET studies over 5 years for a 42-year-old male office worker with dementia resulting from excessive alcohol intake for several years. To the best of our knowledge, there has been no report showing that regional cerebral glucose hypometabolism improves with the amelioration of neuropsychological impairment in a patient with ARD. We discuss the possible neural basis of reversible ARD.

Case Report

A 42-year-old man was admitted to hospital for the evaluation of his slowly progressive impairment in recent memory. He reported that he had been suffering from daily stress at work and forgetfulness for a few years. He complained that he had difficulty in concentrating and thinking and lacked motivation, although he did not report appetite loss or sleep disturbance. For 6 months before admission, his supervisor had recognized that his memory disturbance was becoming worse. Although he made notes to remember some things, he often forgot to write them down. He lost his way home once. He often lost his temper, but sometimes could not remember the reason for his behavior. He gradually became unable to do his work. He had no history of neurological or psychiatric illness. Since he had not revealed a history of excessive alcohol intake, an early stage of Alzheimer's disease was initially suspected, and he was admitted to the hospital for the evaluation of dementia.

On admission, he showed mild cognitive decline and impairment in emotional control and concentration. He appeared to be apathic. In his general and neurological examination, extraocular movements were full and truncal or limb ataxia was not noted. He was slightly disoriented, and his recent memory was definitely disturbed, while his remote memory was relatively preserved. Neuropsychological batteries on admission showed an immediate verbal memory decline. The geriatric depression scale (GDS) revealed the worst possible score (15 points), which indicated that he was in a depressive state (see Neuropsychological Assessment in Results). Blood tests revealed a slight elevation of the levels of aspartate and alanine aminotransferases and triglycerides, thereby suggesting fatty liver. Serum thiamine level (37 ng/mL) was within the normal range (20-50 ng/mL), while serum vitamin B_{12} level was 323 pg/mL(normal range, 249-938 pg/mL). Serological tests for syphilis were negative, and thyroid function was normal. The finding of brain magnetic resonance imaging was unremarkable. Electroencephalography showed generalized intermittent irregular slow waves (theta range). His memory and emotional control improved gradually after admission to hospital. The score of Miyake's Verbal Memory Test improved at 3 weeks after admission as compared to those performed on admission (Table 1). Since his motivation did not improve despite the recovery of memory function, a low dose of an antidepressant (25 mg/day of maprotiline hydrochloride) was started.

One year after discharge, he confessed that he had a history of daily excessive alcohol intake for several years prior to admission. He had consumed 2 drinks/day for several years and 6 drinks/day for 1 year prior to admission (1 drink equals 12 g of pure ethanol; National Institute on Alcohol Abuse and Alcoholism recommends alcohol consumption of $\leq$2 drinks/day for people of similar age) (1, 14). He had abstained from alcohol since admission to hospital, although he had shown no symptoms of withdrawal during hospitalization. This information confirmed the final diagnosis as a reversible type of ARD. To elucidate the pathophysiology of this unique condition, we conducted a follow-up study with FDG-PET and neuropsychological tests for 5

years after hospitalization. At present, the patient is working in a middle management position with no problems at work.

Methods

Neuropsychological tests

The Japanese edition of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) was used for the assessment of intelligence. Miyake's Paired-associated Word Learning Test for Verbal Memory was used as the verbal memory test. In this test, the subject is requested to memorize 10 pairs of either associated or non-associated nouns and immediately recollect the paired word. This procedure is repeated 3 times with a time interval. The results are expressed as the number of words recalled accurately in each procedure (15, 16). The Japanese version of the Geriatric Depression Scale (GDS) was used as the depression scale, although the patient's age was younger than the target age group considered for this scale (17). The Mini-Mental State Examination (MMSE) was used for a simple intelligence scale.

Image data acquisition and analyses

FDG-PET was performed using a General Electric Advance PET scanner (General Electric Medical Systems, Milwaukee, WI, USA). A 370 MBq (10 mCi) of [^{18}F]-FDG was injected intravenously into the patient. Forty minutes after administration of the radiotracer, 35 slices of brain emission images were acquired over a 20-min period. The emission images were reconstructed using an iterative reconstruction method. All reconstructed images were corrected for attenuation by using ^{68}Ge-^{68}Ga transmission scans.

In voxel-wise analyses using SPM2 software (Wellcome Department of Imaging Neuroscience, UCL, London, UK), spatially normalized images were smoothed with an isotopic Gaussian Kernel set at 16-mm full-width at half-maximum (FWHM). To remove the effect of the global count, the count of each voxel was normalized to the total count of the brain by using proportional scaling. The FDG-PET image of the patient was compared with those of 12 age-matched controls (mean age, 37.3 ± 12.9 years) by using *t* statistics. We investigated hypometabolic brain areas for the patient as compared with control subjects. The regions were considered to be significant at a height threshold of p=0.01, uncorrected for multiple comparison (Z score=2.34), and an extent threshold of 50 voxels. For visualization, significant clusters were projected onto a surface-rendered anatomical template provided by SPM2. The spatial coordinates of the local maxima from the statistical analysis were used to identify the corresponding brain areas according to the atlas of Talairach and Tournoux (18). The nonlinear transformation of the Montreal Neurological Institute (MNI) coordinates into the Talairach coordinates was performed using appropriate converter software (mni2tal.m; http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml).

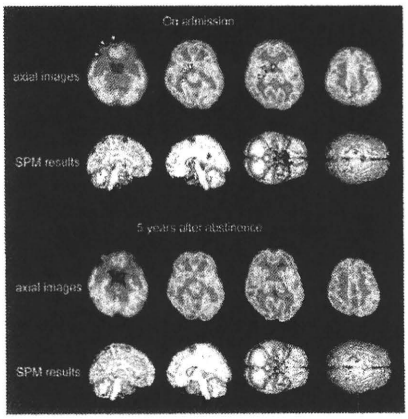

Figure 1. **This figure shows axial images of FDG-PET and the results of the voxel-wise statistical comparison with healthy subjects (n=12) by using SPM2 (height threshold, z>2.34, p<0.01; extent threshold>50 voxels). FDG-PET on admission showed glucose hypometabolism in the right diencephalon, including the anterior thalamus and the bilateral basal forebrains more on the right side (white arrow heads). The SPM results clarified that cerebral glucose hypometabolism improved at 5 years after abstinence in the right diencephalon and bilateral basal forebrains and temporal poles.**

Results

Neuropsychological assessments

As shown in Table 1, a trend of amelioration was found in all neuropsychological batteries. Among these batteries, the score of the nonassociated paired-word test in Miyake's Verbal Memory Test was markedly improved at 5 years after discharge. The depression scale score at 5 years after discharge also showed complete amelioration as compared to that at admission.

FDG-PET analyses by SPM2

As shown in Fig. 1 and Table 2, the voxel-based statistical analysis using SPM2 for the first FDG-PET revealed glucose hypometabolism in the right diencephalon, including the anterior thalamus; the bilateral basal forebrains, temporal poles and supplementary motor areas (SMAs); the dorsal brainstem. The subsequent FDG-PET analysis at 5 years after discharge revealed improvement in cerebral glucose metabolism in the right diencephalon and the bilateral basal forebrains and temporal poles.

Although glucose hypometabolism was still detected to some extent in the temporal pole, SMA and dorsal basal brain stem, magnetic resonance imaging showed no anatomical abnormalities in such regions.

Table 2. Brain Regions of Our Patient Showing a Significant Decrease in Glucose Metabolism in FDG-PET Study on Admission and 5 Years after Abstinence as Compared with Those of the Healthy Subjects

Brain region	Side	Talairach coordinates of the peak			Z score
		x	y	z	
On admission					
Diencephalon	R	12	−2	6	3.94
Temporal pole	L	−24	18	−29	3.91
Orbitofrontal gyrus	R	10	10	24	3.19
Retrosplenium	R	32	−44	21	3.34
SMA	L	−2	3	64	2.85
Dorsal brain stem	−	8	−27	5	2.84
5 years after abstinence					
Temporal pole	L	−24	18	−29	3.14
SMA	L	8	−27	5	2.93
Dorsal brain stem	−	8	−27	5	2.66

R: right, L: left, SMA: supplementary motor cortex

Discussion

Etiopathic brain regions for tentative cognitive decline

The patient had no evidence of alcohol dependency throughout the clinical course, although the patient had a history of excessive alcohol drinking. We consider the patient did not have acute abstinent syndrome, which was originates from not only alcohol but also from drugs, because our patient did not have abstinent syndrome during the hospitalization, and the patient's MMSE score was full. We also consider that acute brain syndrome, like black out, due to excessive alcohol drinking, or caused by repetitive toxicity, might was not seen in the patient, throughout this patient's hospitalization.

In the present patient, cerebral glucose hypometabolism was initially detected in the diencephalon and basal forebrain. Five years of abstinence resulted in improvement in cerebral glucose metabolism in these regions and cognitive function. This might suggest that the tentative hypofunction in these 2 brain regions was ascribed to the reversible nature of cognitive dysfunction in our patient.

The diencephalon and basal forebrain have been associated with amnesic diseases such as WKS or Alzheimer's disease. In WKS, neuropathological changes occur in the memory circuit in the diencephalons such as the anterior nuclei of the thalami, the mammillary bodies, and mammillothalamic tracts (19-22). A more recent FDG-PET study revealed that glucose metabolism is decreased in these brain regions (4). Thus, both the structural and functional changes in the diencephalons are ascribed to the irreversible nature of cognitive decline in WKS (1).

Cognitive impairment in WKS is also ascribed to the cholinergic pathway from the basal forebrain, as in the case of Alzheimer's disease (23). Thiamine is thought to play a role in the cholinergic synaptic transmission and axonal conduction, and an excessive alcohol intake can result in thiamine deficiency (5). In our patient, the cholinergic neurons in the basal forebrain might be impaired tentatively because of either direct toxicity of excessive alcohol or a rapid decrease in thiamine concentration in the blood, although the thiamine concentration was within the normal range.

Although ARD might represent a heterogeneous disease concept, including a variant of WKS, the present case might provide a clue to elucidate the etiopathic brain regions in the reversible type of ARD. It remains to be studied whether the irreversible type of ARD results from the same lesions as those observed in our patient.

Furthermore, regarding the recovery ability of this patient, another important factor for the recovery of cognitive abilities might be cognitive plasticity adaptation after brain damage due to excessive drinking, especially for relatively young patients as in the present case. In the future, it will be necessary to elucidate the mechanism of this plasticity, as few studies have considered this point (24).

Clinical implication

The initial symptoms in the present case included amnesia, slight disorientation, and impairment of emotional control and concentration. These symptoms are compatible with the early stage of Alzheimer's disease according to DSM-IV-TR. While Alzheimer's disease is irreversible, cognitive function in the present patient showed gradual improvement after cessation of alcohol intake on hospitalization. Therefore, we finally diagnosed his illness as ARD.

The proportion of depressive patients among alcoholics is approximately 2 times higher than that among healthy population (25). In the present patient, a complication of depression was also suspected based on the lack of motivation and low GDS score in the initial evaluation. However, his mem-

ory function had already improved at 3 weeks after abstinence when the antidepressant had not yet been administered. In addition, the topography of changes in glucose hypometabolism in our patient differed from those in patients with depression. In patients with depression, glucose hypometabolism in the prefrontal cortices is common, and these areas are associated with neuropsychological impairment (26, 27). The patient had no history of psychiatric disease, including depression, apathy, alcohol dependence, and drug abuse before this alcohol excessive drinking history. Thus, we consider that depression was unlikely the main cause of cognitive decline in our patient, although it might have played a partial role in the recovery from executive dysfunction in his daily life after discharge.

In summary, we report a case of reversible ARD without thiamine deficiency that mimiced Alzheimer's disease. Detailed medical history taking is necessary for the early diagnosis and intervention of this disease. FDG-PET might also facilitate early diagnosis of this disease.

References

1. Sadock BJ, Sadock VA. In: Kaplan & Sadock's Synopsis of Psychiatry: Behavioral Science. Clinical Psychiatry. Lippincott Williams & Wilkins, Philadelphia, 2002.
2. Neiman J. Alcohol as a risk factor for brain damage: neurologic aspects. Alcohol Clin Exp Res **22** (Suppl. 7): 346S-351S, 1998.
3. Victor M, Adams RD, Collins GH. The Wernicke-Korsakoff syndrome and related neurologic disorders due to alcoholism and malnutrition. Davis FA, Ed. Philadelphia, 1989.
4. Reed LJ, Lasserson D, Marsden P, et al. FDG-PET findings in the Wernicke-Korsakoff syndrome. Cortex **39**: 1027-1045, 2003.
5. Sechi G, Serra A. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol **6**: 442-455, 2007.
6. McIntosh C, Chick J. Alcohol and the nervous system. J Neurol Neurosurg Psychiatry **75** (Suppl. 3): 16-21, 2004.
7. Adams KM, Gilman S, Koeppe RA, et al. Neuropsychological deficits are correlated with frontal hypometabolism in positron emission tomography studies of older alcoholic patients. Alcohol Clin Exp Res **17**: 205-210, 1993.
8. Fadda F, Rossetti ZL. Chronic ethanol consumption: from neuroadaptation to neurodegeneration. Progr Neurobiol **56**: 385-431, 1998.
9. Johnson-Greene D, Adams KM, Gilman S, et al. Effects of abstinence and relapse upon neuropsychological function and cerebral glucose metabolism in severe chronic alcoholism. J Clin Exp Neuropsychol **19**: 378-385, 1997.
10. Lishman WA. Alcoholic dementia: a hypothesis. Lancet **1**: 1184-1186, 1986.
11. Lishman WA. Alcohol and the brain. Brit J Psychiatry **156**: 635-644, 1990.
12. Wang GJ, Volkow ND, Hitzemann R, Oster ZH, Roque C, Cestaro V. Brain imaging of an alcoholic with MRI, SPECT, and PET. Am J Physiol Imaging **7**: 194-198, 1992.
13. Wong DF, Maini A, Rousset OG, Brasic JR. Positron emission tomography-a tool for identifying the effects of alcohol dependence on the brain. Alcohol Res Health **27**: 161-173, 2003.
14. Fiellin DA, Reid MC, O'Connor PG. Outpatient management of patients with alcohol problems. Ann Intern Med **133**: 815-827, 2000.
15. Ishiai S, Koyama Y, Seki K, et al. Unilateral spatial neglect in AD: significance of line bisection performance. Neurology **55**: 364-370, 2000.
16. Morino M, Uda T, Naito K, et al. Comparison of neuropsychological outcomes after selective amygdalohippocampectomy versus anterior temporal lobectomy. Epilepsy Behav **9**: 95-100, 2006.
17. Demura S, Sato S, Tada N, Matsuzawa J, Hamasaki H. Agreement in depression determination among four self-rating depression scales applied to Japanese community-dwelling elderly. Envir Health Prev Med **11**: 177-183, 2006.
18. Talairach J, Tournoux P. Co-Planar Stereotaxic Atlas of the Human Brain. Stuttgart: Thieme, 1988.
19. Chick J. Alcohol and the brain. Curr Opin Psychiatry **10**: 205-210, 1997.
20. Harding A, Halliday G, Caine D, Kril J. Degeneration of anterior thalamic nuclei differentiates alcoholics with amnesia. Brain **123**: 141-154, 2000.
21. Harper C. The incidence of Wernicke's encephalopathy in Australia--a neuropathological study of 131 cases. J Neurol Neurosurg Psychiatry **46**: 593-598, 1983.
22. Mair WG, Warrington EK, Weiskrantz L. Memory disorder in Korsakoff's psychosis: a neuropathological and neuropsychological investigation of two cases. Brain **102**: 749-783, 1979.
23. Arendt T, Bigl V, Arendt A, Tennstedt A. Loss of neurons in the nucleus basalis of Meynert in Alzheimer's disease, paralysis agitans and Korsakoff's disease. Acta Neuropathol **61**: 101-108, 1983.
24. Bartsch AJ, Homola G, Biller A, et al. Manifestations of early brain recovery associated with abstinence from alcoholism. Brain **130**: 36-47, 2007.
25. Sullivan LE, Fiellin DA, O'Connor PG. The prevalence and impact of alcohol problems in major depression: a systematic review. Am J Med **118**: 330-341, 2005.
26. Baxter LR Jr, Schwartz JM, Phelps ME, et al. Reduction of prefrontal cortex glucose metabolism common to three types of depression. Arch Gen Psychiatry **46**: 243-250, 1989.
27. Drevets WC. Functional neuroimaging studies of depression: the anatomy of melancholia. Annu Rev Med **49**: 341-361, 1998.