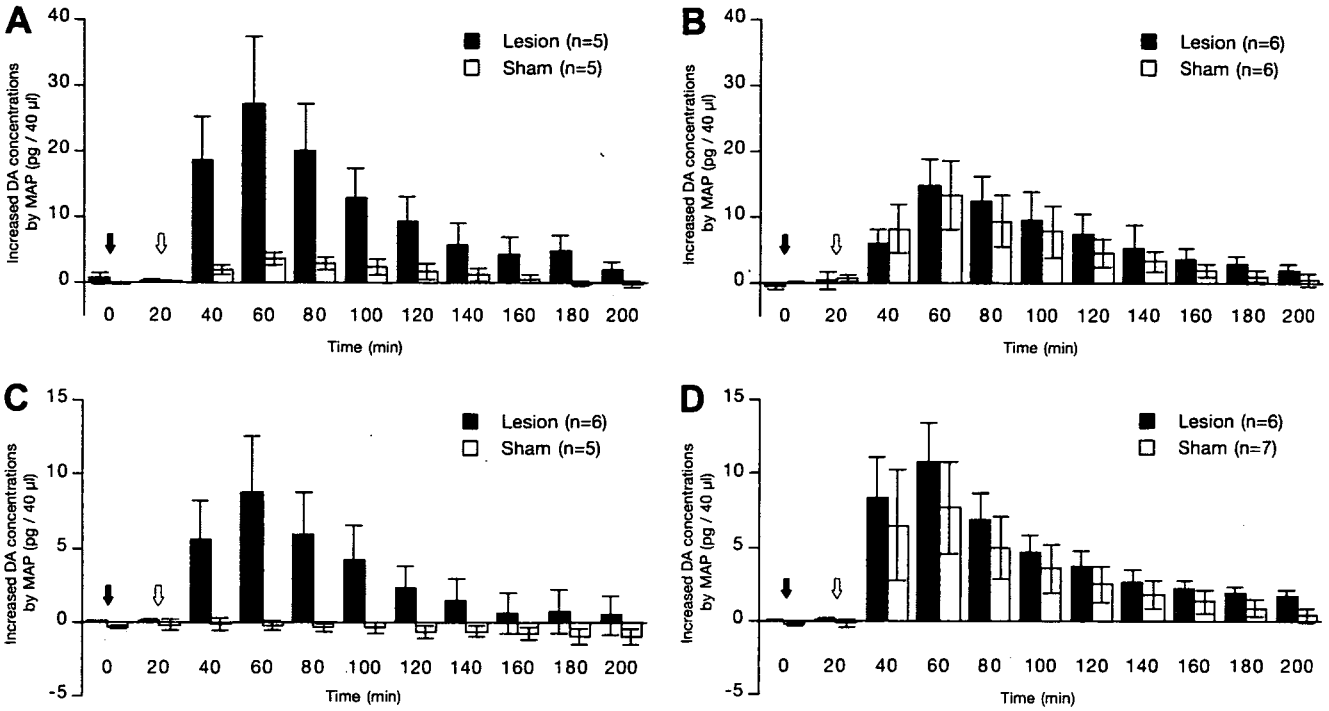

Fig. 3. Time course of the MAP (1.0 mg/kg, i.p.)-induced increase of extracellular DA concentrations in the NAC (**A** and **B**) and in the BLA (**C** and **D**) of sham-operated (open bars) and lesioned (shaded bars) rats. MAP was injected 20 min after lidocaine (A and C) or artificial CSF (B and D) infusion into the mPFC. Arrows indicate the point of drug administration (closed arrows, lidocaine; open arrows, MAP). MAP-induced increase in DA levels was calculated by subtracting the basal DA levels (the mean of three consecutive samples before lidocaine or artificial CSF administration) from MAP-induced DA release. Values are expressed as mean ± SEM.

operation × time interaction effect [$F(9,180) = 0.87$, $P = 0.56$] was not significant (Figs. 3C and 3D).

Effect of EC lesions and mPFC inactivation on MAP-induced locomotor activity

Figure 4 shows MAP-induced locomotor activity. Two-way ANOVA revealed a significant main effect of operation [$F(1.55) = 7.09$, $P = 0.01$] but not injection [$F(1.55) = 1.26$, $P = 0.27$], without a significant operation × injection interaction [$F(1.55) = 1.99$, $P = 0.16$]. The results indicate that EC lesions, but not inactivation of mPFC enhanced locomotion. Subsequent analysis was conducted to examine operation effects in CSF- and lidocaine-injected rats separately. Lidocaine infusion augmented the ability of EC lesions to enhance MAP-induced locomotor activity [$F(1,25) = 5.38$, $P = 0.029$], while CSF infusion did not [$F(1,30) = 1.32$, $P = 0.26$].

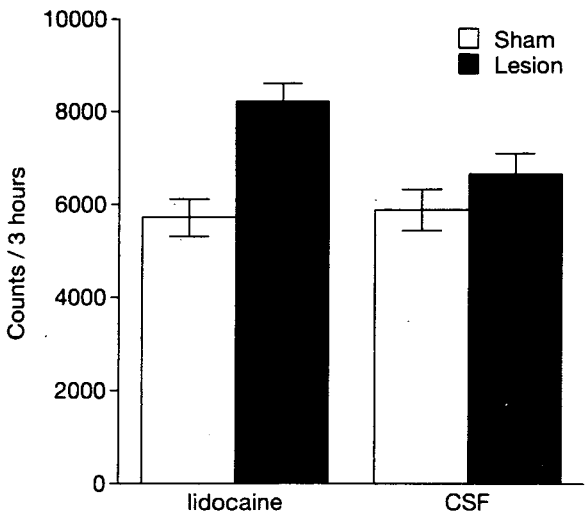

Fig. 4. Locomotor activity of EC lesioned rats (shaded bar; lidocaine infusion $n = 14$, artificial CSF infusion $n = 17$) or sham-operated rats (open bar; lidocaine infusion $n = 17$, artificial CSF infusion $n = 18$) during 3 h after methamphetamine (1.0 mg/kg, i.p.) administration. Lidocaine was infused into the mPFC 20 min before MAP administration. Values are expressed as mean ± SEM. Asterisks indicate a significant difference in comparisons between lesioned and sham-operated rats in each microinjection status (one-way ANOVA).

Effect of EC lesions and mPFC inactivation on PPI

Two-way ANOVA demonstrated no significant main effects of injection [$F(1.51) = 0.23$, $P = 0.63$] and operation [$F(1,55) = 1.02$, $P = 0.32$], as well as their interaction [$F(1,55) = 0.44$, $P = 0.51$] on SA (Fig. 5A).

For PPI, three-way ANOVA indicated a significant main effect of prepulse (74, 78 dB) [$F(1,51) = 8.71$, $P = 0.005$] and operation × prepulse interaction [$F(1,51) = 5.66$, $P = 0.021$]. Subsequent analysis revealed a significant effect of injection [$F(1,51) = 6.58$, $P = 0.013$]. These results indicated that inactivation of mPFC by

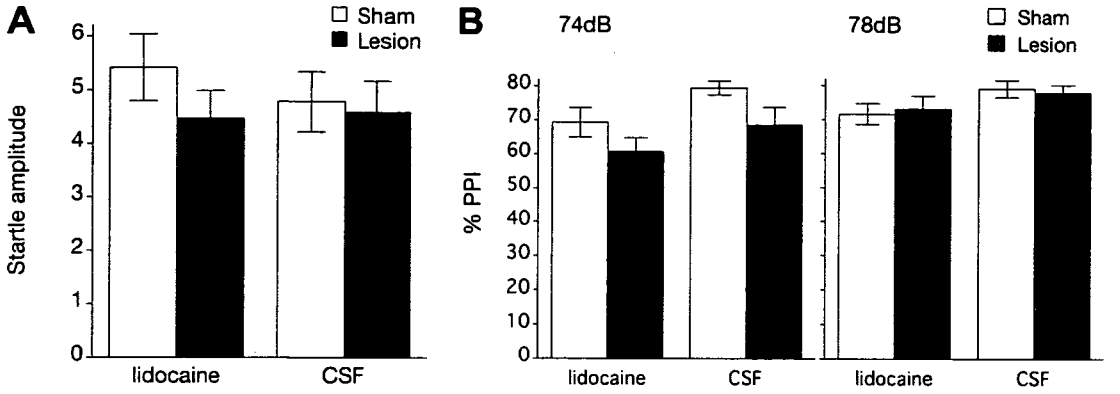

Fig. 5. **A:** Mean amplitudes of startle reflex on the single noise (120 dB) trials during PPI sessions. Data of EC lesioned rats (lidocaine infusion $n = 13$, artificial CSF infusion $n = 13$) are shown by shaded bars and sham-operated rats (lidocaine infusion $n = 17$, artificial CSF infusion $n = 18$) by open bars. Values are expressed as mean ± SEM. **B:** PPI with prepulses of 74 and 78 dB after lidocaine or artificial CSF infusion into the mPFC in EC lesioned rats (shaded bar; lidocaine infusion $n = 13$, artificial CSF infusion $n = 13$) and sham-operated rats (open bar; lidocaine infusion $n = 17$, artificial CSF infusion $n = 18$). Values are expressed as mean ± SEM.

TABLE I. Effects of mPFC inactivation and EC lesions on neurochemical and behavioral parameters

	NAC		BLA			
	Sham	EC-lesion	Sham	EC-lesion	EC- effect on LA	EC-lesion effect on PPI
Artificial CSF infusion					→	↓
Basal DA release	→	→	→	→		
MAP-induced DA release	(+)	(+)	(+)	⇑		
Lidocaine infusion					⇑	⇓
Basal DA release	→	→	↓	↓		
MAP-induced DA release	(+)	⇑	(−)	⇑		

→, no change compared with sham-operated rats; ↓, decrease compared with sham-operated rats; ⇑ and ⇓ significantly greater and lesser enhancement compared with sham-operated counterparts, respectively. mPFC, medial prefrontal cortex; NAC nucleus accumbens; BLA, basolateral amygdale; EC, entorhinal cortex; LA. Locomotor activity; PPI, prepulse inhibition; CSF, cerebrospinal fluid.

lidocaine infusion disrupted PPI, and that EC lesions reduced PPI in with the weaker prepulse (74 dB).

Table I shows the summary of the effects of EC lesions and mPFC inactivation on neurochemical and behavioral parameters.

DISCUSSION

This study was undertaken to determine if inactivation of the mPFC affects mesolimbic DA activity and PPI in rats with EC lesions. The results showed that infusion of lidocaine into the mPFC exhibits differential effects on DAergic neurotransmission in the NAC and BLA (Table I). Moreover, inactivation of the mPFC and EC lesions both disrupted sensorimotor gating, as demonstrated by reduced PPI.

Infusion of lidocaine causes neural inactivation by its local anesthetic effect via blockade of Na^+ channels (Catterall, 1980). The concentration and volume of lidocaine used in the current study was based on previous studies (Lomber, 1999; Tehovnik and Sommer, 1997; Woods and Ettenberg, 2004), which show neural inactivation that lasts 15–60 min (Lomber, 1999; Tehovnik and Sommer, 1997).

The current study demonstrated that lidocaine infusion into the mPFC reduced basal (tonic) DA release, and attenuated MAP (1.0 mg/kg, i.p.)-induced DA release in the BLA in both lesioned and sham-operated rats. The mPFC sends nerve projections to the BLA with glutamate as the transmitter (Brinley-Reed et al., 1995; McDonald, 1998; Sesack et al., 1989). It is possible that acute inactivation of the mPFC causes a decrease in these excitatory inputs, leading to reduced tonic and phasic (MAP-induced) DA release in the BLA. On the other hand, enhancement of MAP-induced DA release in the BLA of EC lesioned rats (Figs. 3C and 3D) is consistent with the results of our previous study (Uehara et al., 2004). Lesioning of EC for 4 weeks is thought to decrease extatory inputs into the BLA. These findings, suggestive of exaggerated phasic DA response, are in line with an increase in tissue concentrations of DA and new DA pool in nerve terminals in the BLA (Uehara et al., 2004), as well as enhancement of stress-induced DA release in the BLA (Uehara et al., 2003) of EC-lesion rats.

The major finding of this study is that inactivation of the mPFC augmented MAP (1.0 mg/kg, i.p.)-induced DA release in the NAC of EC-lesioned, but not sham-operated rats (Figs. 3A and 3B). The mPFC has been shown to regulate DA release in the NAC through its glutamatergic afferents to the ventral tegmental area (VTA) (Karreman and Moghaddam, 1996; Taber and Fibiger, 1995). Infusion of TTX into

the PFC causes a decrease in extracellular DA levels in the NAC (Karreman and Moghaddam, 1996). By contrast, a previous study (Murase et al., 1993) reports that microinfusion of lidocaine into the mPFC transiently reduces DA release in the NAC and burst firing in the VTA, suggesting that basal (tonic) DA release in the NAC is under a tonic excitatory control by the mPFC through glutamatergic projections to the DA cell body in the VTA. The discrepancy between the previous results and the present findings may be ascribed to the difference in the method of inactivation (i.e., TTX in the previous studies vs. lidocaine in this study) and/or other factors.

Stimulation of the BLA has been demonstrated to directly modulate the DA release in the NAC (Howland et al., 2002; Jackson and Moghaddam, 2001; Leonetti et al., 2006). Glutamate release from neurons originating from the BLA and projecting into the NAC has been shown to evoke local DA release in the NAC (Howland et al., 2002; Leonetti et al., 2006). Infusion of lidocaine into the BLA (Woods and Ettenberg, 2004), as well as DA-depleting (6-OHDA) lesions of the BLA (Simon et al., 1988), has been shown to enhance amphetamine-induced locomotor response without affecting spontaneous locomotion. Likewise, an in vivo voltametry study showed that 6-OHDA lesions of the BLA increased the DA signaling in the NAC in response to tail pinch or predor odor stress (Stevenson et al., 2003), although infusion of lidocaine into the mPFC was reported not to block the BLA stimulation-evoked increase in DA release in the NAC (Howland et al., 2002). These results overall suggest that decreasing tonic DA activity in the BLA may enhance phasic DA transmission without significant changes in tonic DAergic activity in the NAC, and that reduced MAP-induced DA release in the BLA may contribute to augmented DAergic activity in the NAC in rats with EC lesions during inactivation of the mPFC.

Left EC lesions significantly increased MAP-induced locomotor activity, replicating the results of our previous study (Sumiyoshi et al., 2004). In that study, the EC lesioned rats did not show a significant change in MAP (1 mg/kg, i.p.)-induced DA release in the NAC compared to sham-operated animals, while the EC lesioned rats exhibited significantly greater MAP-induced locomotor activity than did sham-operated animals (Sumiyoshi et al., 2004). A subsequent study (Sumiyoshi et al., 2005) reports a marked (twofold) increase in the proportion of the high-affinity state of D2 receptors in the striatum of EC lesioned rats without a change in the D1 receptor component. These results indicate supersensitivity of subcortical D2 receptors in rats with excitotoxic damage to the EC (Seeman et al., 2006; Sumiyoshi et al., 2004, 2005). Moreover, the fact that lidocaine-injected rats demonstrated that a greater locomotor activity in the EC lesion rats is consistent with neurochemical data in the current study.

Inactivation of mPFC by lidocaine infusion, as well as EC lesions, reduced PPI without affecting SAs. PPI has been shown to reflect the activation of limbic and cortico–pallido–striato–thalamic circuitry that mediates sensorimotor gating (Koch and Schnitzler, 1997; Swerdlow et al., 2001). DA projections to the NAC are considered to play an important role in mediating PPI (Swerdlow et al., 1990a,b; Zhang et al., 2000). PPI is also modulated by DA transmissions in the BLA, independent of changes in those in the NAC (Stevenson and Gratton, 2004). In the current study, PPI was disrupted by lidocaine infusion into the mPFC. Although basal DA release in the NAC was not changed during inactivation of mPFC (Figs. 2A and 2B), MAP-induced DA release was increased by mPFC inactivation in EC lesioned rats. On the other hand, lidocaine infusion into the mPFC decreased basal DA release in the BLA. Moreover, inactivation of mPFC attenuated MAP-induced DA release. These findings suggest that mPFC inactivation leads to dysfunction of tonic and phasic DAergic neurotransmission in the NAC and BLA, providing a possible mechanism by which mPFC inactivation disrupted PPI.

EC lesions produced disruption of PPI without affecting SAs, similar to the findings in rats with bilateral EC lesions (Goto et al., 2002). In the present study, EC lesions did not change basal DA release in the NAC. On the other hand, EC lesions have been demonstrated to produce an increase in the proportion of the high-affinity state of D2 receptors in the striatum of rats without a change in D1 receptor component (Sumiyoshi et al., 2005). Therefore, it is likely that PPI disruption in the lesion rats was mediated by postsynaptic DA supersensitivity in the NAC of EC lesioned rats (Sumiyoshi et al., 2004). Blockade of D1 and D2/D3 receptors in the BLA has been reported to produce opposite effects on PPI. Thus, PPI is disrupted by D2/D3 receptor antagonists, whereas it is enhanced by D1 receptor blockade (Stevenson and Gratton, 2004). As mentioned above, the lesioned animals do not show a change in the proportion of the high-affinity state of the D3 receptor subtype (Seeman et al., 2006). These results suggest a contribution of supersensitivity of postsynaptic D2 receptors in the BLA to the disruption of PPI in rats with EC lesions. Further studies are warranted to investigate the role for other DA receptor subtypes in impaired sensorimotor gating in animals with EC lesions.

In the present study, lidocaine was infused into the left mPFC in the behavioral experiments (locomotion, PPI) to produce the same condition as in the microdialysis experiments. Because prefrontal cortex connects with the bilateral BLA (Granato et al., 1991), inactivation of the left mPFC may have affected neural activity of not only the ipsilateral but also contra-

lateral BLA. It is worthwhile to investigate the long-term effect of continuous mPFC inactivation on the limbic DAergic neurotransmission and related behaviors in animals with EC lesions.

The volume reduction in the parahippocampal gyrus has been reported to be correlated with the severity of positive psychotic symptoms of schizophrenia (Bogerts, 1997). A morphological study from our laboratory suggests that the severity of Schneiderian symptoms is inversely correlated the left parahippocampal gyrus volumes (Suzuki et al., 2005a). On the other hand, greater PPI has been associated with higher relative metabolic activity rates in prefrontal cortex, as demonstrated by positron emission tomography (Hazlett et al., 1998). Moreover, better attentional modulation of PPI has been associated with higher frontal/occipital ratios of glucose metabolism in healthy subjects, but not patients with schizophrenia (Hazlett and Buchsbaum, 2001). These clinical observations may be relevant to the results presented here, showing that rats with excitotoxic lesions of the left EC and/or inactivation of mPFC elicit abnormal DAergic activity.

In conclusion, the results of this study indicate that inactivation of the mPFC, as well as EC lesions, leads to dysregulation of DAergic transmissions in the limbic regions. The findings that inactivation of the mPFC in rats with EC lesions augmented MAP-induced DA release in the NAC and disrupted PPI may support the hypothesis that dysfunction of prefrontal cortex may play a crucial role in the manifestation of psychosis in subjects with volume reductions in the medial temporal lobe structures (Kurachi, 2003a,b; Siever and Davis, 2004; Suzuki et al., 2005b). Investigations into the functional state of DA receptor subtypes in the EC lesion rats under mPFC inactivation are warranted to further examine the construct validity of these rats as an animal model of psychosis vulnerability (Seeman et al. 2006; Sumiyoshi et al. 2004, 2005).

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REFERENCES

Andreasen NC, O'Leary DS, Flaum M, Nopoulos P, Watkins GL, Boles Ponto LL, Hichwa RD. 1997. Hypofrontality in schizophrenia: Distributed dysfunctional circuits in neuroleptic-naive patients. Lancet 349:1730–1734.

Bogerts B. 1997. The temporolimbic system theory of positive schizophrenic symptoms. Schizophr Bull 23:423–435.

Bogerts B, Meertz E, Schonfeldt-Bausch R. 1985. Basal ganglia and limbic system pathology in schizophrenia. A morphometric study of brain volume and shrinkage. Arch Gen Psychiatry 42:784–791.

Bogerts B, Ashtari M, Degreef G, Alvir JM, Bilder RM, Lieberman JA. 1990. Reduced temporal limbic structure volumes on magnetic resonance images in first episode schizophrenia. Psychiatry Res 35:1–13.

Brinley-Reed M, Mascagni F, McDonald AJ. 1995. Synaptology of prefrontal cortical projections to the basolateral amygdala: An electron microscopic study in the rat. Neurosci Lett 202:45–48.

Carlsson A. 1988. The current status of the dopamine hypothesis of schizophrenia. Neuropsychopharmacology 1:179–186.

Catterall WA. 1980. Neurotoxins that act on voltage-sensitive sodium channels in excitable membranes. Annu Rev Pharmacol Toxicol 20:15–43.

Degreef G, Ashtari M, Bogerts B, Bilder RM, Jody DN, Alvir JM, Lieberman JA. 1992. Volumes of ventricular system subdivisions measured from magnetic resonance images in first-episode schizophrenic patients. Arch Gen Psychiatry 49:531–537.

Falkai P, Bogerts B, Rozumek M. 1988. Limbic pathology in schizophrenia: The entorhinal region—A morphometric study. Biol Psychiatry 24:515–521.

Goto K, Ueki A, Iso H, Morita Y. 2002. Reduced prepulse inhibition in rats with entorhinal cortex lesions. Behav Brain Res 134:201–207.

Goto Y, O'Donnell P. 2004. Prefrontal lesion reverses abnormal mesoaccumbens response in an animal model of schizophrenia. Biol Psychiatry 55:172–176.

Grace AA. 1991. Phasic versus tonic dopamine release and the modulation of dopamine system responsivity: A hypothesis for the etiology of schizophrenia. Neuroscience 41:1–24.

Grace AA. 2000. Gating of information flow within the limbic system and the pathophysiology of schizophrenia. Brain Res Brain Res Rev 31:330–341.

Granato A, Santarelli M, Minciacchi D. 1991. Bihemispheric organization of amygdalo-cortical projections in the rat. Neurosci Lett 127:53–56.

Harrison PJ. 1999. The neuropathology of schizophrenia. A critical review of the data and their interpretation. Brain 122(Part 4):593–624.

Hazlett EA, Buchsbaum MS. 2001. Sensorimotor gating deficits and hypofrontality in schizophrenia. Front Biosci 6:D1069–D1072.

Hazlett EA, Buchsbaum MS, Haznedar MM, Singer MB, Germans MK, Schnur DB, Jimenez EA, Buchsbaum BR, Troyer BT. 1998. Prefrontal cortex glucose metabolism and startle eyeblink modification abnormalities in unmedicated schizophrenia patients. Psychophysiology 35:186–198.

Howland JG, Taepavarapruk P, Phillips AG. 2002. Glutamate receptor-dependent modulation of dopamine efflux in the nucleus accumbens by basolateral, but not central, nucleus of the amygdala in rats. J Neurosci 22:1137–1145.

Jackson ME, Moghaddam B. 2001. Amygdala regulation of nucleus accumbens dopamine output is governed by the prefrontal cortex. J Neurosci 21:676–681.

Karreman M, Moghaddam B. 1996. The prefrontal cortex regulates the basal release of dopamine in the limbic striatum: An effect mediated by ventral tegmental area. J Neurochem 66:589–598.

Kawasaki Y, Maeda Y, Urata K, Higashima M, Yamaguchi N, Suzuki M, Takashima T, Ide Y. 1993. A quantitative magnetic resonance imaging study of patients with schizophrenia. Eur Arch Psychiatry Clin Neurosci 242:268–272.

Kawasaki Y, Suzuki M, Nohara S, Hagino H, Takahashi T, Matsui M, Yamashita I, Chitnis XA, McGuire PK, Seto H, Kurachi M. 2004. Structural brain differences in patients with schizophrenia and schizotypal disorder demonstrated by voxel-based morphometry. Eur Arch Psychiatry Clin Neurosci 254:406–414.

Koch M, Schnitzler HU. 1997. The acoustic startle response in rats—Circuits mediating evocation, inhibition and potentiation. Behav Brain Res 89:35–49.

Kurachi M. 2003a. Pathogenesis of schizophrenia. I. Symptomatology, cognitive characteristics and brain morphology. Psychiatry Clin Neurosci 57:3–8.

Kurachi M. 2003b. Pathogenesis of schizophrenia. II. Temporo-frontal two-step hypothesis. Psychiatry Clin Neurosci 57:9–15.

Kurachi M, Sumiyoshi T, Shibata R, Sun Y-J, Uehara T, Tanii Y, Suzuki M. 2000. Changes in limbic dopamine metabolism following quinolinic acid lesions of the left entorhinal cortex in rats. Psychiatry Clin Neurosci 54:83–89.

Lawrie SM, Abukmeil SS. 1998. Brain abnormality in schizophrenia. A systematic and quantitative review of volumetric magnetic resonance imaging studies. Br J Psychiatry 172:110–120.

Leonetti M, Desvignes C, Bougault I, Souilhac J, Oury-Donat F, Steinberg R. 2006. 2-Chloro-*N*-[(S)-phenyl [(2S)-piperidin-2-yl] methyl]-3-trifluoromethyl benzamide, monohydrochloride, an inhibitor of the glycine transporter type 1, increases evoked-dopamine release in the rat nucleus accumbens in vivo via an enhanced glutamatergic neurotransmission. Neuroscience 137:555–564.

Liddle PF, Friston KJ, Frith CD, Hirsch SR, Jones T, Frackowiak RS. 1992. Patterns of cerebral blood flow in schizophrenia. Br J Psychiatry 160:179–186.

Lipska BK, Al-Amin HA, Weinberger DR. 1998. Excitotoxic lesions of the rat medial prefrontal cortex: Effects on abnormal behaviors associated with neonatal hippocampal damage. Neuropsychopharmacology 19:451–464.

Lomber SG. 1999. The advantages and limitations of permanent or reversible deactivation techniques in the assessment of neural function. J Neurosci Methods 86:109–117.

McDonald AJ. 1998. Cortical pathways to the mammalian amygdala. Prog Neurobiol 55:257–332.

Murase S, Grenhoff J, Chouvet G, Gonon FG, Svensson TH. 1993. Prefrontal cortex regulates burst firing and transmitter release in rat mesolimbic dopamine neurons studied in vivo. Neurosci Lett 157:53–56.

Paxinos G, Watson C. 1998. The rat brain in stereotaxic coordinates. Sydney: Academic Press.

Roberts GW. 1991. Schizophrenia: A neuropathological perspective. Br J Psychiatry 158:8–17.

Seeman P, Schwarz J, Chen JF, Szechtman H, Perreault M, McKnight GS, Roder JC, Quirion R, Boksa P, Srivastava LK, Yanai K, Weinshenker D, Sumiyoshi T. 2006. Psychosis pathways converge via D2 (high) dopamine receptors. Synapse 60:319–346.

Selemon LD, Kleinman JE, Herman MM, Goldman-Rakic PS. 2002. Smaller frontal gray matter volume in postmortem schizophrenic brains. Am J Psychiatry 159:1983–1991.

Sesack SR, Deutch AY, Roth RH, Bunney BS. 1989. Topographical organization of the efferent projections of the medial prefrontal cortex in the rat: An anterograde tract-tracing study with *Phaseolus vulgaris* leucoagglutinin. J Comp Neurol 290:213–242.

Shenton ME, Dickey CC, Frumin M, McCarley RW. 2001. A review of MRI findings in schizophrenia. Schizophr Res 49:1–52.

Siever LJ, Davis KL. 2004. The pathophysiology of schizophrenia disorders: Perspectives from the spectrum. Am J Psychiatry 161:398–413.

Simon H, Taghzouti K, Gozlan H, Studler JM, Louilot A, Herve D, Glowinski J, Tassin JP, Le Moal M. 1988. Lesion of dopaminergic terminals in the amygdala produces enhanced locomotor response to d-amphetamine and opposite changes in dopaminergic activity in prefrontal cortex and nucleus accumbens. Brain Res 447:335–340.

Stevenson CW, Gratton A. 2004. Role of basolateral amygdala dopamine in modulating prepulse inhibition and latent inhibition in the rat. Psychopharmacology (Berl) 176:139–145.

Stevenson CW, Sullivan RM, Gratton A. 2003. Effects of basolateral amygdala dopamine depletion on the nucleus accumbens and medial prefrontal cortical dopamine responses to stress. Neuroscience 116:285–293.

Sumiyoshi T, Tsunoda M, Uehara T, Tanaka K, Itoh H, Sumiyoshi C, Kurachi M. 2004. Enhanced locomotor activity in rats with excitotoxic lesions of the entorhinal cortex, a neurodevelopmental animal model of schizophrenia: Behavioral and in vivo microdialysis studies. Neurosci Lett 364:124–129.

Sumiyoshi T, Seeman P, Uehara T, Itoh H, Tsunoda M, Kurachi M. 2005. Increased proportion of high-affinity dopamine D2 receptors in rats with excitotoxic damage of the entorhinal cortex, an animal model of schizophrenia. Brain Res Mol Brain Res 140:116–119.

Suzuki M, Zhou SY, Hagino H, Niu L, Takahashi T, Kawasaki Y, Matsui M, Seto H, Ono T, Kurachi M. 2005a. Morphological brain changes associated with Schneider's first-rank symptoms in schizophrenia: A MRI study. Psychol Med 35:549–560.

Suzuki M, Zhou SY, Takahashi T, Hagino H, Kawasaki Y, Niu L, Matsui M, Seto H, Kurachi M. 2005b. Differential contributions of prefrontal and temporolimbic pathology to mechanisms of psychosis. Brain 128(Part 9):2109–2122.

Swerdlow NR, Braff DL, Masten VL, Geyer MA. 1990a. Schizophrenic-like sensorimotor gating abnormalities in rats following dopamine infusion into the nucleus accumbens. Psychopharmacology (Berl) 101:414–420.

Swerdlow NR, Mansbach RS, Geyer MA, Pulvirenti L, Koob GF, Braff DL. 1990b. Amphetamine disruption of prepulse inhibition of acoustic startle is reversed by depletion of mesolimbic dopamine. Psychopharmacology (Berl) 100:413–416.

Swerdlow NR, Geyer MA, Braff DL. 2001. Neural circuit regulation of prepulse inhibition of startle in the rat: Current knowledge and future challenges. Psychopharmacology (Berl) 156:194–215.

Taber MT, Fibiger HC. 1995. Electrical stimulation of the prefrontal cortex increases dopamine release in the nucleus accumbens of the rat: Modulation by metabotropic glutamate receptors. J Neurosci 15(5 Part 2):3896–3904.

Tehovnik EJ, Sommer MA. 1997. Effective spread and timecourse of neural inactivation caused by lidocaine injection in monkey cerebral cortex. J Neurosci Methods 74:17–26.

Uehara T, Tanii Y, Sumiyoshi T, Kurachi M. 2000. Neonatal lesions of the left entorhinal cortex affect dopamine metabolism in the rat brain. Brain Res 860:77–86.

Uehara T, Sumiyoshi T, Itoh H, Kurachi M. 2003. Modulation of stress-induced dopamine release by excitotoxic damage of the entorhinal cortex in the rat. Brain Res 989:112–116.

Uehara T, Sumiyoshi T, Itoh H, Kurachi M. 2004. Inhibition of dopamine synthesis with α-methyl-p-tyrosine abolishes the enhancement of methamphetamine-induced extracellular dopamine levels in the amygdala of rats with excitotoxic lesions of the entorhinal cortex. Neurosci Lett 356:21–24.

Woods VE, Ettenberg A. 2004. Increased amphetamine-induced locomotion during inactivation of the basolateral amygdala. Behav Brain Res 149:33–39.

Zhang J, Forkstam C, Engel JA, Svensson L. 2000. Role of dopamine in prepulse inhibition of acoustic startle. Psychopharmacology (Berl) 149:181–188.

Zhou SY, Suzuki M, Hagino H, Takahashi T, Kawasaki Y, Matsui M, Seto H, Kurachi M. 2005. Volumetric analysis of sulci/gyri-defined in vivo frontal lobe regions in schizophrenia: Precentral gyrus, cingulate gyrus, and prefrontal region. Psychiatry Res 139:127–139.

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Prevalence of large cavum septi pellucidi and its relation to the medial temporal lobe structures in schizophrenia spectrum

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Abstract

Magnetic resonance imaging was used to evaluate the prevalence of the cavum septi pellucidi (CSP) in 154 schizophrenia patients, 47 schizotypal disorder patients, and 163 healthy controls. We also explored the relation of a large CSP (≥6 mm) with medial temporal lobe structures. No significant difference was found in the prevalence of the CSP (76.0% of the schizophrenia patients, 81.6% of the controls, and 85.1% of the schizotypal patients) or the large CSP (6.5% of the schizophrenia patients, 7.4% of the controls, and 10.6% of the schizotypal patients) among the groups, but patients with a large CSP (10 schizophrenia and 5 schizotypal patients) had smaller volumes of bilateral amygdala and left posterior parahippocampal gyrus than patients without it. In the control subjects, the large CSP did not affect the volumes of the medial temporal lobe structures. These findings might reflect neurodevelopmental abnormalities in midline and associated limbic structures of the brain in schizophrenia spectrum.

Keywords: Amygdala; Cavum septi pellucidi; Magnetic resonance imaging; Schizophrenia; Schizotypal disorder

1. Introduction

Septum pellucidi is a component of the limbic system and plays a crucial role in the connection between the hypothalamus and the hippocampus, amygdala, habenula, and brain-stem reticular formation (Sarwar, 1989). The cavum septi pellucidi (CSP), which is caused by an incomplete fusion of the septum pellucidi, is thought to be a normal anatomical variant, but unusually large CSP has been implicated in fetal neurodevelopmental abnormalities and its presence might reflect abnormalities in the development of the corpus callosum and limbic system structures including the amygdala and hippocampus (Bodensteiner and Schaefer, 1990; Rakic and Yakovlev, 1968; Sarwar, 1989; Shaw and Alvord, 1969).

Several magnetic resonance imaging (MRI) studies in schizophrenia have reported an increased prevalence of the large CSP (de Souza Crippa et al., 2006; Nopoulos et al., 1997, 1998) and its relation to the morphologic changes of the medial temporal lobe structures (Kasai et al., 2004; Kwon et al., 1998). These findings in schizophrenia may reflect the abnormal neurodevelopment in midline and associated limbic structures (Sarwar, 1989), while not consistently replicated (Flashman et al., 2007; Keshavan et al., 2002a,b; Rajarethinam et al.,

Abbreviations: ANOVA, Analysis of variance; CASH, Comprehensive Assessment of Symptoms and History; CSP, Cavum septi pellucidi; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; ICC, Intraclass correlation coefficient; ICD-10, International Classification of Diseases, 10th edition; ICV, Intracranial volume; MANCOVA, Multivariate analysis of covariance; MRI, Magnetic resonance imaging; SCID-II, Structured Clinical Interview for DSM-IV axis II disorders; SPD, Schizotypal personality disorder.

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2001). Also in our previous study using high-resolution MRI (Hagino et al., 2001), we failed to find a higher prevalence of the large CSP in schizophrenia patients despite a relatively large sample size (86 patients and 79 healthy comparisons). The difference in the prevalence of the large CSP between schizophrenia patients and healthy subjects, if present, is considered to be relatively small, and more cases of a large CSP would be required to elucidate the implications of this abnormality in schizophrenia.

Pathological deviations genetically and phenomenologically related to schizophrenia are grouped under the schizophrenia spectrum. This concept reflects the assumption that schizophrenia has a multifactorial aetiology in which multiple susceptibility genes interact with environmental insults to yield a range of phenotypes (Siever and Davis, 2004). Schizotypal (personality) disorder (SPD) is thought to be a prototypic disorder within the schizophrenia spectrum (Siever et al., 2002), characterized by odd behavior and attenuated forms of schizophrenic features without the manifestation of an overt and sustained psychosis (American Psychiatric Association, 1994; World Health Organization, 1992). It is genetically related to schizophrenia (Kendler et al., 1993; Siever et al., 1990) and might share neurodevelopmental abnormalities with schizophrenia as a common neurobiological basis for vulnerability factors as part of the schizophrenia spectrum. To our knowledge, however, only two MRI studies have evaluated the CSP in schizotypal subjects, where a trend toward an elevated rate of a large CSP was found in a relatively small sample of SPD subjects (Dickey et al., 2007; Kwon et al., 1998).

In this study, we used MRI to evaluate the prevalence of the CSP in an extended sample of normal controls and schizophrenia patients as well as in schizotypal disorder patients. We also investigated the relation between the large CSP and medial temporal lobe structures in a sub-sample of schizophrenia spectrum disorders and healthy controls. On the basis of our previous study (Hagino et al., 2001) and hypothesized abnormal neurodevelopment in midline and medial temporal lobe structures in schizophrenia (Kasai et al., 2004; Kwon et al., 1998), we predicted that the prevalence of the large CSP would not differ among the groups, but that it would affect the medial temporal morphology.

2. Methods

2.1. Subjects

Demographic and clinical data of the subjects in this study are presented in Table 1. This cohort includes 86 schizophrenia patients and 79 healthy controls investigated in our former CSP study (Hagino et al., 2001). All subjects were right-handed and physically healthy at the time of the study, and none had a lifetime history of serious head trauma, neurological illness, serious medical or surgical illness, or substance abuse. The three groups were matched for age, gender, and height.

One hundred fifty-four schizophrenia patients (79 inpatients and 75 outpatients) who met the ICD-10 criteria for research (World Health Organization, 1993) were recruited from the inpatient and outpatient clinics of the Department of Neuropsychiatry, Toyama University Hospital. Diagnoses were made following structured clinical interviews by psychiatrists with the Comprehensive Assessment of Symptoms and History (CASH; Andreasen et al., 1992). One hundred forty-eight patients were receiving neuroleptic medication; 90 were being treated with typical neuroleptics and 58 were receiving atypical neuroleptics. Clinical symptoms were rated by well-trained psychiatrists at the time of scanning using the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984) and the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984).

Forty-seven schizotypal disorder patients were recruited from among the patients who visited the clinics with schizotypal features accompanied by distress or associated problems in their lives. The sample characteristics of the clinic-based schizotypal subjects in our laboratory have been described in detail elsewhere (Takahashi et al., 2006). Structured clinical interviews were performed using the CASH (Andreasen et al., 1992) and Structured Clinical Interview for DSM-IV axis II disorders

Table 1
Clinical and demographic characteristics of patients with schizophrenia, patients with schizotypal disorder, and normal control subjects[a]

	Schizophrenia patients	Schizotypal patients	Control subjects
	$N=154$	$N=47$	$N=163$
	($N=69$)	($N=36$)	($N=72$)
Male/female	74/80	29/18	97/66
	(35/34)	(24/12)	(43/29)
Age (years)	28.0 ±7.8	25.0±5.4	27.0±8.0
	(26.3±5.7)	(25.8±5.4)	(24.9±5.9)
Height (cm)	163.8±7.6	165.9±8.7	165.7±8.2
	(164.6±7.7)	(165.9±9.0)	(166.9±7.3)
Education (years)	13.0±2.0	13.1±2.0	15.9[b]±2.7
	(13.5±1.9)	(13.6±1.8)	(16.2[b]±2.6)
Parental education (years)	12.2±2.3	12.3±1.7	13.1[c]±2.6
	(12.0±2.1)	(12.2±1.8)	(13.0[c]±2.5)
Age at onset (years)	23.0±6.4	–	–
	(21.8±4.3)	(–)	(–)
Duration of illness (years)	5.1±5.5	–	–
	(4.6±5.1)	(–)	(–)
Duration of medication	3.6[d]±4.7	1.5±3.0	–
(years)	(3.5[d]±4.3)	(1.8±3.3)	(–)
Drug	10.3[d]±8.4	4.8±5.7	–
(mg/day, haloperidol equiv.)	(11.6[d]±9.3)	(4.2 ± 4.7)	(–)
Total SAPS score	26.9[d]±21.8	15.9±9.3	–
	(25.9[d]±20.4)	(16.6±9.0)	(–)
Total SANS score	49.6[e]±21.2	41.9±22.6	–
	(46.7±23.1)	(42.6±22.9)	(–)

The values represent means± SDs. SANS, Scale for the Assessment of Negative Symptoms (Andreasen, 1984); SAPS, Scale for the Assessment of Positive Symptoms (Andreasen, 1984).
ANOVA followed by Scheffé's test was used.
[a] The values in parentheses show the data of the sub-sample for whom volumetric data were available.
[b] $p<0.01$: compared to the schizophrenia and schizotypal patients.
[c] $p<0.05$: compared to the schizophrenia patients.
[d] $p<0.01$: compared to the schizotypal patients.
[e] $p<0.05$: compared to the schizotypal patients.

(SCID-II) (First et al., 1997). They all met the criteria for schizotypal disorder in the ICD-10 (World Health Organization, 1993) as well as the criteria for schizotypal personality disorder in the DSM-IV (American Psychiatric Association, 1994). Based on the data from the CASH and SCID-II, subjects were diagnosed by the consensus of at least two experienced psychiatrists. All subjects have received consistent clinical follow-up. One male subject has developed schizophrenia after scanning, but none of the other schizotypal subjects has developed overt psychosis to date (mean follow-up period after MRI scanning=2.9 years, SD=2.5). Thirty-four patients were outpatients, and the other 13 underwent closer clinical and medical examinations including MRI during short-term admission. At the time of MRI scanning, 40 of the 47 patients were treated with low-dose antipsychotics, of which 14 were treated with typical neuroleptics and 26 received atypical neuroleptics. The remaining six patients were neuroleptic-naïve. Clinical symptoms were rated at the time of scanning using the SANS and SAPS.

The controls subjects consisted of 163 healthy volunteers recruited from among members of the community, hospital staff, and university students. They were given a questionnaire consisting of 15 items concerning their family and past histories, as well as present illness. They did not have any personal or family history of psychiatric illness in their first-degree relatives. The control subjects were not screened with a standard measure such as a SCID-II and this may be a possible limitation of the study. However, all control candidates were interviewed and administered the Minnesota Multiphasic Personality Inventory (MMPI) by experienced clinical psychologists in order to obtain a rather homogeneous control group without eccentric profiles on the MMPI. Although the MMPI has not proved very sensitive for the detection of schizotypy (Walters, 1983), approximately 17% of the candidates for normal controls were excluded for having an abnormal profile with a *T*-score for the validity scales or the clinical scales exceeding 70.

Volumetric measurements of the medial temporal lobe structures were available for 69 schizophrenia patients, 36 schizotypal patients, and 72 controls (Table 1). This subgroup included 137 subjects from our previous study (Suzuki et al., 2005), which investigated the medial temporal and frontal lobe structures in the schizophrenia spectrum, and an additional 40 subjects; all the subjects with a large CSP in our entire sample (10 schizophrenia patients, 5 schizotypal patients, and 12 controls) were enrolled in the volumetric analysis in order to explore the relation of a large CSP with medial temporal lobe structures. The characteristics of this sub-sample seem to be largely comparable with those of the whole sample of the present study (Table 1). However, this cohort was somewhat younger than the whole sample, since we included relatively young schizophrenia patients and age-matched controls for the volumetric analyses in order to reduce the confounds in the data due to the medication and chronicity of illness. This study was approved by the Committee on Medical Ethics of University of Toyama. After a complete description of the study, written informed consent was obtained from all subjects.

2.2. MRI data acquisition and image analysis

MRI scans were acquired with a 1.5-T scanner (Vision; Siemens Medical System, Erlangen, Germany). A three-dimensional T1-weighted gradient-echo sequence FLASH (fast low-angle shots) with 1×1×1 mm voxels was used. Imaging parameters were: TE=5 ms; TR=24 ms; flip angle=40°, field of view=256 mm; matrix size=256×256. The image data were transferred to a Unix workstation (Silicon Graphics, Inc., Mountain View, CA, USA) and processed using the software package Dr View 5.3 (AJS, Tokyo, Japan). Brain images were realigned in three dimensions and reconstructed into entire contiguous coronal images, with a 1-mm thickness, perpendicular to the intercommissural line. The intracranial volume (ICV) was measured to correct for differences in head size as previously described (Zhou et al., 2003); the three groups for whom volumetric data were available did not significantly differ in their ICV volumes [repeated measures multivariate analysis of covariance (MANCOVA) with age and height as covariates, $F=1.39$, $df=2, 172$, $p=0.251$].

For the assessment of the CSP, the number of coronal slices where a cavum was seen was counted (Hagino et al., 2001; Nopoulos et al., 1997, 1998). Since the images were 1-mm thick without gap, the rating was a reflection of the actual anterior-to-posterior length of the cavum. A CSP equal to or greater than 6 mm in length was defined as large. All images were assessed by one rater (TT) without any knowledge of the subjects' identity, gender, or diagnosis. Inter-(TT and HH) and intra-rater intraclass correlation coefficients (ICC) in 30 randomly selected brains were over 0.97 for ratings of the CSP.

The amygdala, hippocampus, and parahippocampal gyrus were manually traced on 1-mm consecutive coronal slices with the corresponding sagittal and axial planes simultaneously presented for reference. The procedures for delineation of these structures were described in detail previously (Niu et al., 2004; Suzuki et al., 2005). The inferior border of the amygdala in contact with the hippocampus head was determined by reference to the sagittal plane; the alveus was used to differentiate these structures. The parahippocampal gyrus was subdivided into anterior and posterior parts at the level of the posterior edge of the mammillary body. Three trained raters (TT, HH, and LN), who were blinded to the subjects' identity, gender, diagnosis, and information about the CSP (length, large or non-large), measured the volumes of these structures. Inter- and intra-rater ICCs in five randomly selected brains were over 0.90.

2.3. Statistical analysis

Chi-square tests, or Fisher's exact tests when expected cell sizes were less than five, were used for assessing the frequency of the CSP. To explore the relation of a large CSP ($\geq$6 mm) with medial temporal lobe structures in a sub-sample for whom volumetric data were available, relative volumes (100×absolute volume/ICV) were analyzed using a repeated measures multivariate analysis of covariance (MANCOVA) for each ROI, with age, duration of neuroleptic medication, and medication dosage as covariates, diagnosis [schizophrenia spectrum patients

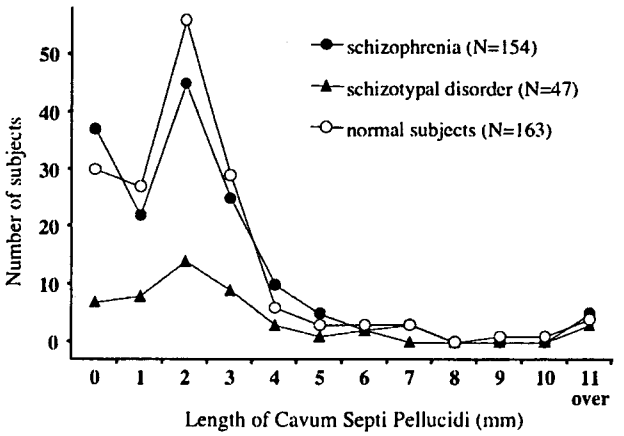

Fig. 1. Length of the cavum septi pellucidi (CSP) in patients with schizophrenia, patients with schizotypal disorder, and normal control subjects. No difference was found in the prevalence of the CSP among the three groups.

(schizophrenia and schizotypal disorder patients) versus controls] and CSP (large versus non-large CSP) as between-subject factors, and hemisphere as a within-subject variable. Since patients with schizophrenia are the main clinical group of interest, the relation between the large CSP and medial temporal lobe structures was also analyzed for only schizophrenia patients and controls. The volumetric measures for all ROIs in this study were normally distributed (tested by Kolmogorov–Smirnov test). The post hoc Scheffé's test was employed.

For patients with schizophrenia spectrum disorders, the relationships between the length of the CSP and relative volumes of the medial temporal lobe structures were examined by Pearson's partial correlation coefficients controlling for potential confounders such as age, duration of neuroleptic medication, and medication dosage. For these analyses, the subjects without CSP (12 schizophrenia and 4 schizotypal patients) were regarded as having a CSP of 0.5 mm and then the length of the CSP was log-transformed because of their skewed distribution. Statistical significance was defined as $P<0.05$ (two-tailed).

3. Results

The prevalence of the CSP was 76.0% (117/154) in the schizophrenia patients, 81.6% (133/163) in the controls, and 85.1% (40/47) in the schizotypal patients (Fig. 1), showing no group differences (chi-square=2.53, $p=0.28$). No difference was found in the prevalence of the large CSP among the diagnostic groups [6.5% (10/154) of the schizophrenia patients, 7.4% (12/163) of the controls, and 10.6% (5/47) of the schizotypal patients] ($p=0.64$, Fisher's exact probability test). There was no significant gender difference in the prevalence of the CSP or a large CSP in any of the diagnostic groups.

For the relationship between the large CSP and the medial temporal lobe structures (Table 2), MANCOVA of amygdala volume revealed a significant diagnosis-by-CSP interaction, with the subjects who had a large CSP having bilaterally smaller amygdala volumes than the subjects without a large CSP for the schizophrenia spectrum patients (Scheffé's test, $p<0.001$) but not for the control subjects (Scheffé's test, $p=0.996$). A significant diagnosis-by-CSP-by-hemisphere interaction for the volume of the posterior parahippocampal gyrus was also demonstrated ($F=8.07$, $df=1$, 173, $p=0.005$); the patients with schizophrenia spectrum disorders with a large CSP had a smaller left posterior parahippocampal gyrus than did the patients without a large CSP (Scheffé's test, $p<0.001$), while there was no difference in the volume of the left posterior parahippocampal gyrus between controls with and without a large CSP (Scheffé's test, $p=1.000$). When only the schizophrenia patients and controls were included in the analyses, we also found a significant diagnosis-by-CSP interaction for the relative volume of the amygdala ($F=7.41$, $df=1$, 134,

Table 2
Absolute volume for regions of interest in subjects with or without a large cavum septi pellucidi (CSP)[a]

	Healthy controls		Schizophrenia spectrum patients		Analysis of covariance ($df=1$, 170)[b]					
	Non-large CSP	Large CSP	Non-large CSP	Large CSP	Effect of CSP		Effect of diagnosis		Diagnosis×CSP	
Brain region (cm^3)	($N=60$)	($N=12$)	($N=90$)	($N=15$)	F	P	F	P	F	P
Amygdala					7.45	0.007	32.15	<0.001	5.85	0.017
Left	1.12±0.14	1.18±0.12	0.99±0.15	0.84±0.11						
Right	1.15±0.14	1.15±0.10	1.02±0.16	0.94±0.16						
Hippocampus					0.38	0.537	2.88	0.091	0.13	0.715
Left	3.01±0.41	3.14±0.41	2.84±0.39	2.93±0.42						
Right	3.21±0.36	3.28±0.65	3.07±0.43	3.00±0.44						
Anterior PHG					1.53	0.218	0.00	0.973	0.04	0.844
Left	2.40±0.59	2.73±0.62	2.48±0.47	2.81±0.43						
Right	2.78±0.58	2.94±0.46	2.76±0.55	2.87±0.55						
Posterior PHG					4.83	0.029	2.16	0.143	0.63	0.430
Left	4.71±0.56	4.78±0.84	4.67±0.67	4.25±0.60						
Right	4.50±0.45	4.44±0.61	4.39±0.55	4.45±0.53						

CSP, cavum septi pellucidi; PHG, parahippocampal gyrus.
Values represent means±SDs.
[a] The absolute volumes are shown in the table, but the statistical analyses reported here are based on the relative volumes (100×absolute volume/intracranial volume).
[b] Diagnosis-by-CSP-by-hemisphere interaction was observed only for the posterior parahippocampal gyrus.

$p=0.007$) and a significant diagnosis-by-CSP-by-hemisphere interaction for the relative volume of the posterior parahippocampal gyrus ($F=8.10$, $df=1$, 137, $p=0.005$). The post hoc Scheffé's tests showed that the schizophrenia patients with a large CSP had smaller volumes of bilateral amygdala ($p<0.001$) and left posterior parahippocampal gyrus ($p=0.012$) than the patients without it. The effect involving the CSP was not significant for the other regions measured in this study.

Based on the results of the above-mentioned MANCOVA analyses, the correlational analyses between the length of the CSP and ROI volumes were adopted only for the bilateral amygdala and left posterior parahippocampal gyrus in schizophrenia spectrum patients in order to prevent possible type I error. The length of the CSP (log) was negatively correlated with the relative volumes of the amygdala (left, $r=-0.319$, $p=0.001$; right, $r=-0.222$, $p=0.025$) and left posterior parahippocampal gyrus ($r=-0.356$, $p<0.001$).

4. Discussion

In this study, no difference was found in the prevalence of the CSP or a large CSP between the large sample of schizophrenia patients, schizotypal disorder patients, and healthy controls. However, the volumes for bilateral amygdala and the left posterior parahippocampal gyrus in patients with schizophrenia spectrum disorders (schizophrenia and schizotypal disorder combined) were significantly smaller in those who had a large CSP than in those who did not.

The present finding of a high prevalence of the CSP, which is caused by an incomplete fusion of the septum pellucidi during fetal development, in all diagnostic groups supports the notion that the CSP itself is a normal anatomical variant (Nopoulos et al., 1997; Sarwar, 1989). On the other hand, an abnormally large CSP has been implicated in a midline neurodevelopmental anomaly involving a limbic system structure though definition of the large CSP as well as its clinical importance has not been established (Sarwar, 1989). We did not find an increased prevalence in schizophrenia or schizotypal patients compared with control subjects, while several (de Souza Crippa et al., 2006; Kasai et al., 2004; Kwon et al., 1998; Nopoulos et al., 1997) but not all (Flashman et al., 2007; Keshavan et al., 2002a,b; Rajarethinam et al., 2001) studies using high-resolution MRI have reported an increased prevalence of a large CSP in schizophrenia. The reason for these discrepancies is unclear because most studies used basically the same definition for a large CSP (≥ 6 mm), but the current study could be strengthened by the larger sample size compared with those in previous studies that reported an increased prevalence of a large CSP in schizophrenia (29 to 38 patients). The wide variance in the prevalence of a large CSP in schizophrenia reported to date (approximately from 4 to 30%) could be partly explained by differences in imaging techniques or sample characteristics (e.g., race, gender) among the reports. For schizotypal personality disorder patients, previous data indicated that a large CSP is relatively common [5/20 (25%) female (Dickey et al., 2007) and 3/16 (18.8%) male (Kwon et al., 1998) patients]. Although we failed to replicate these findings, abnormalities in midline structures in the schizophrenia spectrum seem worthy of further examination in a larger sample.

Regarding the relation of a large CSP with medial temporal lobe morphology in the schizophrenia spectrum, the patients with a large CSP had a significantly smaller bilateral amygdala than the patients without it. The left posterior parahippocampal gyrus was also smaller in the patients with a large CSP. These findings are consistent with previous MRI studies showing a similar association between a large CSP and volume of the left parahippocampal gyrus (Kasai et al., 2004) or bilateral amygdala–hippocampal complex (Kwon et al., 1998) in schizophrenia. In normal development, the CSP is consistently present in prematures but begins to close just before term and its prevalence is 15% at 3–6 months of birth (Sarwar, 1989; Shaw and Alvord, 1969). Although it is not clear what causes the obliteration of the CSP in most individuals several months after birth, Sarwar (1989) hypothesized that fusion of the septum pellucidi might be caused by rapid growth of the corpus callosum and the limbic system structures such as the hippocampus and amygdala. A reduction in the volume of the medial temporal lobe is suggested to have already occurred at the onset

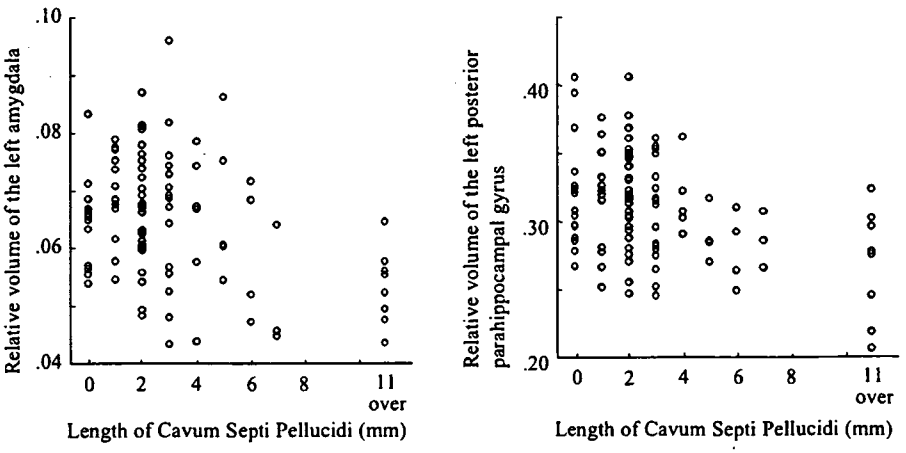

Fig. 2. Scatter plots for the length of the cavum septi pellucidi and relative volumes of the left amygdala and left posterior parahippocampal gyrus in patients with schizophrenia spectrum disorders.

of schizophrenia (Shenton et al., 2001) and has been identified also in subjects at genetic high-risk of developing schizophrenia (Keshavan et al., 2002a,b; Lawrie et al., 2001; Seidman et al., 2002) or in schizotypal subjects (Dickey et al., 2007; Suzuki et al., 2005). These findings are consistent with the neurodevelopmental model of schizophrenia (Weinberger, 1987) and suggest that abnormalities in the medial temporal lobe structures might indicate genetic vulnerability to schizophrenia. The distribution of the length of the CSP and its relation to the medial temporal morphology in this study (Fig. 2) might suggest that there is no obvious threshold effect between large (≥6 mm) and non-large (<6 mm) CSP on the volume of the medial temporal lobe structures in schizophrenia spectrum, and explicitly how neurodevelopmental abnormalities in the medial temporal lobe structures affect the process of the obliteration of the CSP in schizophrenia is obscure. Nevertheless, the present findings support a possible relationship between the neurodevelopment of the septum pellucidi and other limbic structures, and suggest that the presence of a large CSP could be a marker of the neurodevelopmental abnormalities in midline structures as well as related limbic structures, especially the amygdala, which may play an important role in the pathogenesis of schizophrenia (Kurachi, 2003).

A few possible confounding factors in this study need to be addressed. First, we did not separately investigate the relation of an abnormal CSP with the medial temporal lobe structures for schizophrenia and schizotypal disorder because of the small number of patients with a large CSP. Although the results were essentially the same even when we included only the schizophrenia patients and controls in the analyses, the neurobiological similarities and differences in the midline and associated limbic structures between established schizophrenia and a milder form of schizophrenia spectrum disorders remain to be further elucidated. Second, most patients in this study were on neuroleptic medication, which might affect the brain morphology. However, the dosage or duration of neuroleptic medication was not correlated with any of the volumetric measurements of the medial temporal lobe structures or the length of the CSP in either schizophrenia or schizotypal disorder patients.

5. Conclusion

We did not find an increased prevalence of the CSP or a large CSP in schizophrenia or schizotypal patients as compared with control subjects. However, the patients with a large CSP had significantly smaller volumes for bilateral amygdala and left posterior parahippocampal gyrus than the patients without it, possibly reflecting the neurodevelopmental abnormalities in midline and associated limbic structures of the brain in the schizophrenia spectrum.

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References

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.

Andreasen NC. Scale for the assessment of negative symptoms/scale for the assessment of positive symptoms [manual]. Iowa City: University of Iowa Press; 1984.

Andreasen NC, Flaum M, Arndt S. The Comprehensive Assessment of Symptoms and History (CASH): an instrument for assessing diagnosis and psychopathology. Arch Gen Psychiatry 1992;49:615–23.

Bodensteiner JB, Schaefer GB. Wide cavum septum pellucidum: a marker of disturbed brain development. Pediatr Neurol 1990;6:391–4.

de Souza Crippa JA, Zuardi AW, Busatto GF, Sanches RF, Santos AC, Araujo D, et al. Cavum septum pellucidum and adhesio interthalamica in schizophrenia: an MRI study. Eur Psychiatry 2006;21:291–9.

Dickey CC, McCarley RW, Xu ML, Seidman LJ, Voglmaier MM, Niznikiewicz MA, et al. MRI abnormalities of the hippocampus and cavum septi pellucidi in females with schizotypal personality disorder. Schizophr Res 2007;89:49–58.

First MB, Gibbon M, Spitzer RL, Williams JBW, Benjamin LS. Structures clinical interview for DSM-IV axis II personality disorders (SCID-II). Washington DC: American Psychiatric Publishing; 1997.

Flashman LA, Roth RM, Pixley HS, Cleavinger HB, McAllister TW, Vidaver R, et al. Cavum septum pellucidum in schizophrenia: clinical and neuropsychological correlates. Psychiatry Res 2007;154:147–55.

Hagino H, Suzuki M, Kurokawa K, Mori K, Nohara S, Takahashi T, et al. Magnetic resonance imaging study of the cavum septi pellucidi in patients with schizophrenia. Am J Psychiatry 2001;158:1717–9.

Kasai K, McCarley RW, Salisbury DF, Onitsuka T, Demeo S, Yurgelun-Todd D, et al. Cavum septi pellucidi in first-episode schizophrenia and first-episode affective psychosis: an MRI study. Schizophr Res 2004;71:65–76.

Kendler KS, McGuire M, Gruenberg AM, O'Hare A, Spellman M, Walsh D. The Roscommon Family Study. I. Methods, diagnosis of probands, and risk of schizophrenia in relatives. Arch Gen Psychiatry 1993;50:527–40.

Keshavan MS, Dick E, Mankowski I, Harenski K, Montrose DM, Diwadkar V, et al. Decreased left amygdala and hippocampal volumes in young offspring at risk for schizophrenia. Schizophr Res 2002a;58:173–83.

Keshavan MS, Jayakumar PN, Diwadkar VA, Singh A. Cavum septi pellucidi in first-episode patients and young relatives at risk for schizophrenia. CNS Spectr 2002b;7:155–8.

Kurachi M. Pathogenesis of schizophrenia: Part II. Temporo-frontal two-step hypothesis. Psychiatry Clin Neurosci 2003;57:9–15.

Kwon JS, Shenton ME, Hirayasu Y, Salisbury DF, Fischer IA, Dickey CC, et al. MRI study of cavum septi pellucidi in schizophrenia, affective disorder, and schizotypal personality disorder. Am J Psychiatry 1998;155:509–15.

Lawrie SM, Whalley HC, Abukmeil SS, Kestelman JN, Donnelly L, Miller P, et al. Brain structure, genetic liability, and psychotic symptoms in subjects at high risk of developing schizophrenia. Biol Psychiatry 2001;49:811–23.

Niu L, Matsui M, Zhou SY, Hagino H, Takahashi T, Yoneyama E, et al. Volume reduction of the amygdala in patients with schizophrenia: a magnetic resonance imaging study. Psychiatry Res 2004;132:41–51.

Nopoulos P, Swayze V, Flaum M, Ehrhardt JC, Yuh WT, Andreasen NC. Cavum septi pellucidi in normals and patients with schizophrenia as detected by magnetic resonance imaging. Biol Psychiatry 1997;41:1102–8.

Nopoulos PC, Giedd JN, Andreasen NC, Rapoport JL. Frequency and severity of enlarged cavum septi pellucidi in childhood-onset schizophrenia. Am J Psychiatry 1998;155:1074–9.

Rajarethinam R, Miedler J, DeQuardo J, Smet CI, Brunberg J, Kirbat R, et al. Prevalence of cavum septum pellucidum in schizophrenia studied with MRI. Schizophr Res 2001;48:201–5.

Rakic P, Yakovlev PI. Development of the corpus callosum and cavum septi in man. J Comp Neurol 1968;132:45–72.

Sarwar M. The septum pellucidum: normal and abnormal. AJNR Am J Neuroradiol 1989;10:989–1005.

Seidman LJ, Faraone SV, Goldstein JM, Kremen WS, Horton NJ, Makris N, et al. Left hippocampal volume as a vulnerability indicator for schizophrenia: a magnetic resonance imaging morphometric study of nonpsychotic first-degree relatives. Arch Gen Psychiatry 2002;59:839–49.

Shaw CM, Alvord Jr EC. Cava septi pellucidi et vergae: their normal and pathological states. Brain 1969;92:213–23.

Shenton ME, Dickey CC, Frumin M, McCarley RW. A review of MRI findings in schizophrenia. Schizophr Res 2001;49:1–52.

Siever LJ, Davis KL. The pathophysiology of schizophrenia disorders: perspectives from the spectrum. Am J Psychiatry 2004;161:398–413.

Siever LJ, Silverman JM, Horvath TB, Klar H, Coccaro E, Keefe RS, et al. Increased morbid risk for schizophrenia-related disorders in relatives of schizotypal personality disordered patients. Arch Gen Psychiatry 1990;47:634–40.

Siever LJ, Koenigsberg HW, Harvey P, Mitropoulou V, Laruelle M, Abi-Dargham A, et al. Cognitive and brain function in schizotypal personality disorder. Schizophr Res 2002;54:157–67.

Suzuki M, Zhou SY, Takahashi T, Hagino H, Kawasaki Y, Niu L, et al. Differential contributions of prefrontal and temporolimbic pathology to mechanisms of psychosis. Brain 2005;128:2109–22.

Takahashi T, Suzuki M, Zhou SY, Tanino R, Hagino H, Kawasaki Y, et al. Morphologic alterations of the parcellated superior temporal gyrus in schizophrenia spectrum. Schizophr Res 2006;83:131–43.

Walters GD. The MMPI and schizophrenia: a review. Schizophr Bull 1983;9:226–46.

Weinberger DR. Implications of normal brain development for the pathogenesis of schizophrenia. Arch Gen Psychiatry 1987;44:660–9.

World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.

World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: World Health Organization; 1993.

Zhou SY, Suzuki M, Hagino H, Takahashi T, Kawasaki Y, Nohara S, et al. Decreased volume and increased asymmetry of the anterior limb of the internal capsule in patients with schizophrenia. Biol Psychiatry 2003;54:427–36.

特集❖触法精神障害者のアセスメントと治療

鹿児島県における司法精神医学の現状と課題
―司法精神医学教育システムおよびネットワークの確立に向けて―

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抄録：本邦では，司法精神医学の研究や教育に携わる機関が乏しいとの指摘があるように，鹿児島県(本県)でも系統だった教育システムは確立されていない。そこで，今回，アンケート調査を実施し，本県における司法精神医学の現状と課題について検討した。さらに，司法精神医学教育システムおよび，そのネットワーク作りに必要な具体的な方策を抽出した。その結果，本県では現状のままで，今後増加が予想される精神鑑定業務には対応できることが判明した。司法精神医学教育に関しては，鑑定医の養成のみならず，卒前教育の段階からカリキュラムなどを検討する必要があると思われた。また，鑑定医の技能向上のためにも，医療関係者と司法関係者の意見交換の場を設定し，司法精神医学教育の中核的施設・部署の設置を推進していく必要があると考えられた。最後に，今回は具体的に事例の提示を行わなかったが，医療観察法が適用された事例を検証することは，精神医療水準の向上，法律の適切な運用，さらに司法精神医学教育に有益であることを示唆した。

臨床精神医学36：1083～1091

Key words：司法精神医学(forensic psychiatry)，精神鑑定(psychiatric evidence)，医療観察法(mentally disordered offenders)，医学教育(medical education)，刑事訴訟法(criminal proceedings)

1 はじめに

本邦では，司法精神医学の研究や教育に携わる機関が乏しいとの指摘があるように[7)]，鹿児島県(以下，本県)でも司法精神鑑定(以下，精神鑑定)業務は限られた一部の精神科医が個人の責任で請け負い，自らの臨床経験に基づいて，またときには鑑定および精神科臨床の経験を積んだ上級医師に指導・助言を仰ぎながら，半ば独学に近い形で行ってきた。さらに，「心神喪失等の状態で重大

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Current status and the tasks of forensic psychiatry in Kagoshima prefecture, Japan

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な他害行為を行った者の医療および観察などに関する法律」(以下,医療観察法)が施行された現在,刑事訴訟法上の精神鑑定業務に加えて本法の業務が加わることで,これらの精神科医の負担が増加することが予想された。

このような現状を踏まえて,筆者らは平成17年,本県における司法精神医学人材育成のための系統だった教育システムを確立する目的で,精神鑑定業務を担当した一部の精神科医を対象として司法精神医学教育および精神鑑定業務に関する予備的調査を実施した[1]。その結果,本県では,現状のまま一部の精神科医が精神鑑定業務を担当することでほぼ対応できることが明らかになった。しかし,アンケートの内容からは,系統的教育を受けていないまま,司法領域の業務を担当することへの不安が示されるとともに,司法精神医学教育システムが本県においては確立されていない実状を憂慮する意見が認められた[1]。

そこで,今回は,司法精神医学教育システムおよび,そのネットワーク構築に必要な具体的な方策を抽出し実施する目的で,一部修正を加えたアンケート調査を行った。すなわち,前回より調査対象者および対象期間を拡大し,本県でも導入が可能な意見を抽出し,今後の司法精神医学人材育成に関して検討を行った。なお,アンケート調査は,無記名とし,鑑定内容に関する質問項目に関しては,被鑑定人が特定されることがないような倫理面への配慮を行った。

2 研究方法

鹿児島大学病院も含めた本県全域の精神科病院51施設,精神科を標榜する医院・クリニック17施設および精神保健関連の2施設のうち,事前に承諾の得られた7施設に表1に示したようなアンケート用紙を送付した。精神鑑定例は,アンケート調査時点で担当している精神鑑定も網羅できるように平成18年度も含んだ過去10カ年,すなわち平成9年4月1日～平成18年3月31日までの期間に担当した事例を対象とした。さらに,司法精神医学教育や医療観察法に関する自由意見を求める形式の質問も併せて行った。

3 結果

アンケートに回答した医師は,精神鑑定業務を担当した経験のある24名(男性:23名,女性:1名)であった。年齢層は,30歳代が3名,40歳代が9名,50歳代が7名,60歳代が3名,70歳以上が2名であった。勤務先別にみると,大学病院に所属している医師が6名,公立病院に所属している医師が4名,精神科病院に所属している医師が8名,医院・クリニックに所属している医師が5名,その他の施設に所属している医師が1名であった。

精神鑑定業務を行った医師の精神科臨床経験年数は,10～14年が6名,15～19年が3名,20～24年が5名,25～29年が6名,30年以上が4名であった。また,全員が精神保健指定医であった。

図1には,明確な回答が得られた19名の医師が担当した精神鑑定の件数と種類を示した。本県では,限られた一部の精神科医が精神鑑定業務を担当しているわけであるが,図1に示すように,その一部の精神科医の中でも担当した件数については,1件～50数件とばらつきがあった。担当した精神鑑定の内容に関しても,起訴前簡易精神鑑定(以下,簡易鑑定)のみ担当している医師,簡易鑑定と比較すると起訴前嘱託精神鑑定(以下,本鑑定)の割合が圧倒的に少ない医師,逆にその割合が圧倒的に多い医師,公判鑑定が多い医師などばらつきが認められた。

図2には明確な回答が得られた医師を対象とし,精神鑑定の件数および種類を年代別・所属機関別に示した。10年間の対象期間中に所属が異動となった医師に関しては,精神鑑定を担当した時点での所属機関の件数に含めて表記した。これによると,大学病院が41件(本鑑定13件,簡易鑑定26件,公判鑑定2件),公立病院が64件(本鑑定4件,簡易鑑定57件,公判鑑定3件),精神科病院が3件(本鑑定1件,簡易鑑定1件,公判鑑定1件)であった。なお,医院・クリニックに関しては,医師が開業後に,精神鑑定を担当した例がなかったため表記しなかった。

精神鑑定業務を初めて担当した時点での,精神

表1 アンケート用紙

(1) 回答される先生の性別と年齢についてご記入下さい。
性別：①男 ②女
年齢：①20歳代 ②30歳代 ③40歳代 ④50歳代 ⑤60歳代 ⑥70歳以上

(2) 回答される先生の職場についてご記入下さい。
①大学病院 ②公立病院 ③精神科病院 ④医院・クリニック ⑤その他

(3) 回答される先生の精神科経験年数をご記入下さい。
（ ）年目

(4) 回答される先生の精神保健指定資格の有無および資格取得後の年数をご記入下さい。
①ある（ ）年目 ②なし

(5) 回答される先生が過去10年間に担当した司法精神鑑定の件数をご記入下さい。
a. 起訴前簡易鑑定 （ ）件
b. 起訴前嘱託鑑定（本鑑定） （ ）件
c. 公判鑑定 （ ）件
＊鑑定書の提出年月日が，平成9年4月1日から現在の間であった事例。現在担当している事例も含む。

(6) 回答される先生が司法精神鑑定を初めて担当した時点での精神科経験年数と，その鑑定の種類をご記入ください。
（ ）年目 a. 起訴前簡易鑑定 b. 起訴前委託鑑定（本鑑定） c. 公判鑑定

(7) 回答される先生が医療観察法における精神鑑定を担当した件数をご記入下さい。
（ ）件

(8) 精神鑑定業務を行うに際し，修正すべき点がありましたらご記入下さい。
（医療観察法の精神鑑定も含む）
（例：検察官との連携，鑑定料，時間的制約など）

(9) 司法精神医学の教育において，必要と思われることをご記入下さい。
（例：講演会の開催，事例検討会，研修会への参加など）

(10) 現在の日常生活を継続するという条件で，司法精神鑑定は年間何件引き受けることが可能かご記入下さい。
a. 起訴前簡易鑑定 （ ）件
b. 起訴前嘱託鑑定（本鑑定） （ ）件
c. 公判鑑定 （ ）件

(11) 司法精神医学の教育システムを確立していく上で何かご意見がありましたらご記入下さい。

(12) 医療観察法について，何か感想がありましたらご記入下さい。

(13) 鑑定した事例の事件名，性別，年齢，鑑定結果，その後の処遇について可能であれば記載してください。
（記入欄が足りない場合はコピーしてご記入下さい）

事件名	提出年月日	年齢・性別（鑑定開始時）	鑑定の種類（簡易・本鑑定〈起訴前・公判〉，医療観察法など）	犯行時の鑑定結果（例：有責，心神耗弱，心神喪失）	その後の処遇（知り得た範囲で）	鑑定担当時の所属機関

科臨床経験年数と，その際の鑑定の種類については，簡易鑑定は10年以下が3名，11～15年が4名，16～20年が1名，21年以上が1名であった。一方，本鑑定を10年以下で担当した医師はおらず，11～15年が5名，21年以上が1名であった。また，初めての精神鑑定で，公判鑑定を担当した医師が2名いた。なお，初めて担当した精神鑑定としては，簡易鑑定が圧倒的に多く，10年未満という短い精神科臨床経験でも担当していた。

平成17年に施行された医療観察法における精

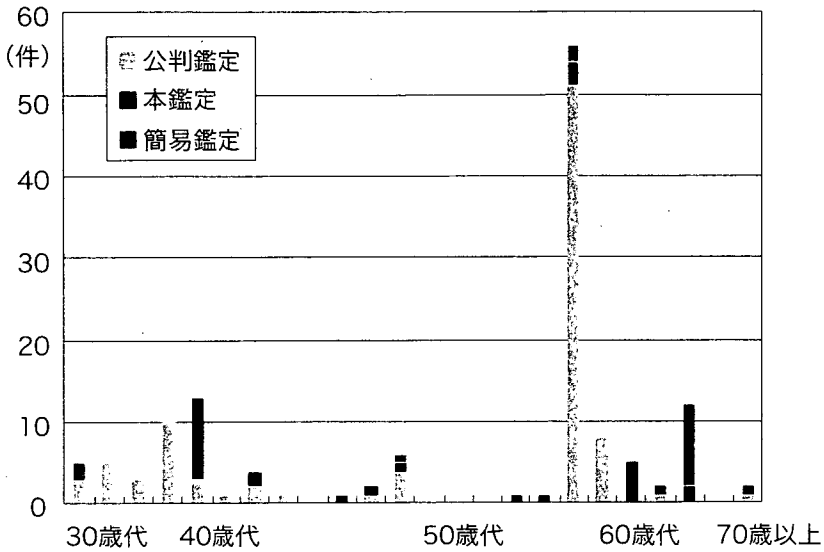

図1　アンケートに回答した医師が過去10年間に担当した司法精神鑑定業務の件数・種類

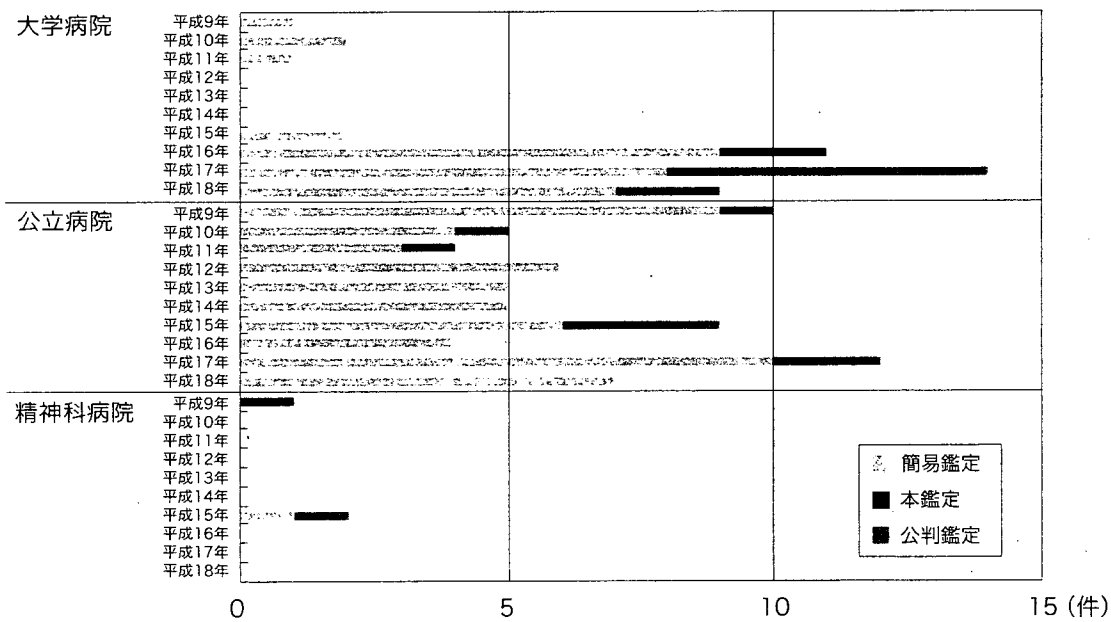

図2　年代・所属機関別の司法精神鑑定件数・種類

神鑑定については，調査した時点で6名の医師が担当しており，そのうち1名は，2件の鑑定業務を担当していた。ただし，この件数は，本県における医療観察法の適用状況のすべてを反映しているものではない。

次に，今後，増加が予想される精神鑑定業務について，それが実際に増えた場合，現状のままで対応できるか否かを予測する目的で，年間に引き受けることが可能な精神鑑定の種類と，その件数について質問を行ったが，その回答結果を図3に示した。

図4には，起訴前精神鑑定の結果と，その後の処遇について示した。明確な回答が得られたうち，触法精神障害者107名中，「心神喪失」と判断された者が44名(44.1%)，「心神耗弱」と判断された者が27名(25.2%)，「有責」と判断された者が36名(33.6%)であった。また，公判鑑定では，いずれも懲役刑が下されていた。しかし，被告人の判決に精神鑑定の結果が反映されたか否かについては不明であった。これは起訴前精神鑑定でも同様で

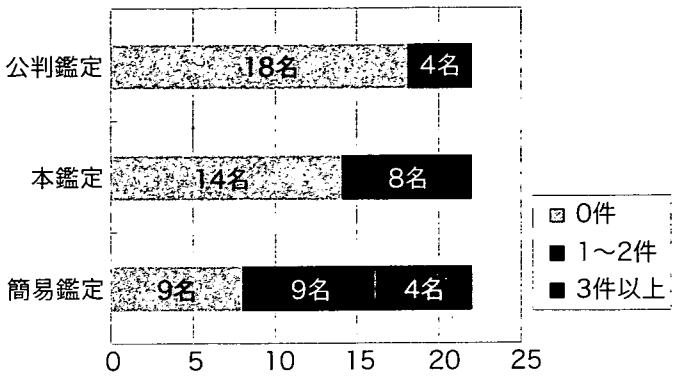

図3　年間に引き受けることが可能な司法精神鑑定の件数・種類

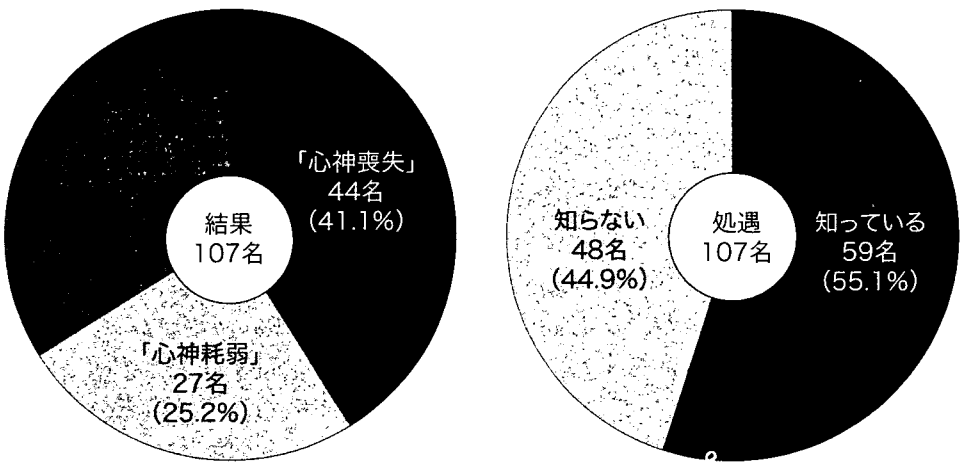

図4　起訴前精神鑑定の結果と被鑑定人の処遇

あり，被疑者が，その後どのように処遇されたのか，ということに関しては，鑑定人本人が「知らない」とする事例が48例あり，これは全体の半数に近い44.9%を占めていた。

最後に，自由な意見を求める形式で質問した内容について示すが，これは筆者ら自身の考えではなく，あくまでもアンケートで得られた自由な意見であることを付記しておく。

まず，「精神鑑定を行うに際して改善すべき点」については，①時間的な制約が大きいため，それに見合う報酬が望ましい，②通常の業務を行いながら，何回も拘置所に行くため診療業務に支障が生じることがある，③検察官によって調査資料が異なり，鑑定開始後に鑑定人が新たに調査依頼をしなければならないほど資料が乏しいことがある，④キーパーソンの供述調書がなかったり，学籍簿がないなど犯行前の資料が乏しいことがある，⑤鑑定書作成の効率を良くするために，資料の電子化を検討してほしい，⑥簡易鑑定でもCTやMRIなどの検査に費やす費用を認めてほしい，⑦鑑定終了後の被疑者の処遇について，検察側からフィードバックがない，⑧司法精神鑑定は，面接および鑑定書作成にかなり時間を要するため，診療時間を割いて鑑定面接に出向く時間的余裕がなく，報酬面から考えても鑑定を引き受ける動機づけとしては乏しい，といったことが自由に記載された意見であった。

次に，「司法精神医学の教育において必要と思われること」，「司法精神医学の教育システムを確立していく上で必要と思われること」に関しては，重複する内容が多かったため，一括して表2に「本アンケートに記載された自由な意見－司法精神医学教育に関して－」として表記した。

一方，「医療観察法についての感想」については，少数ながらもさまざまな意見が記載されていた。すなわち，①指定入院機関の整備を進めるべ

表2 本アンケートに記載された自由な意見
―司法精神医学教育に関して―

- 検察官，裁判官，医療関係者が一同に会する研修会の開催。
- 判定困難な事例などの検討会の開催。
- 参考図書の紹介。
- 専門家による講演会の開催。
- 警察，検察庁，弁護士，消防，行政，県立・民間病院長，大学精神科医局等による精神保健ネットワークの形成。
- 大学等の教育機関でのカリキュラムを見直し，司法精神医学に関する教育を卒前から行っていく必要がある。
- 研修会の開催は，大学病院が主導で行ってほしい。
- 鑑定を担当する医師は，後輩医師を鑑定助手として，鑑定技術の指導を行っていくべきではないか。

きである，②鑑定入院期間中に発生した身体合併症への対応を整備し，移送システムを作ってほしい，③鑑定入院期間中の保安員の配備を検討してほしい，④「治療反応性」という観点から対象外とされている精神遅滞や認知症が疑われる事例にも適用されていることに疑問を感じる，⑤医療観察法の制度下では監視重視に傾き，社会復帰を促す精神保健福祉法との間に齟齬をきたすのではないか，⑥精神保健審判員，精神保健判定医にこだわらず，推薦する形で医療観察法の精神鑑定を引き受けてもらいたい，⑦申し立てがあった場合，裁判官が単独で受理するか否かを決めのはどうかと思う，といったことなどが本アンケートに自由に記載された意見であった。

以上をまとめると，精神鑑定業務を実際に担当した際，資料が不足していることを指摘している意見や，通常業務が時間的にかなり制約されるということも含めて鑑定業務の効率化を求める意見がみられた。次項で詳述するが，業務内容のわりに報酬が低いことを指摘している意見もみられた。司法精神医学教育に関しては，事例検討会や研修会の開催を求める意見が多かった。また，触法精神障害者に接する可能性のある関係機関が参画し，移送も含めたネットワーク作りを求める意見があった。司法精神医学教育システムの確立については，総じて必要であるとする意見が多く，精神鑑定のみならず，触法精神障害者の処遇なども含めて，それらを統括する施設・部署の設置，司法精神医学教育のネットワーク作りを求める意見がみられた。

平成17年から施行された医療観察法に関しては，本県で実際に対象者が発生したこともあってか，鑑定入院期間中に併発した身体疾患への対応の問題[1]や，医療観察法の対象外とされている精神遅滞や認知症が疑われる事例にも適用されていることに対し，「治療反応性」[2]という観点から疑問を指摘する意見もみられた。さらに，合議体による判断で運用される医療観察法が，実際に検察官から申請がなされた段階では裁判官の単独の判断で受理するか否かが決定されていることへの疑問を指摘する意見もみられた。

4 考察

本県における精神鑑定業務は，一部の精神科医が担当しているわけであるが，アンケート調査の結果，鑑定件数および内容ともに，前年度の調査でのばらつきが，より顕著となった。まず，件数としては，本年度も含む10年間で1件にとどまっている医師がいる一方では，50数件に及ぶ医師もいた。これは，精神鑑定の経験年数や，それに対処できるという医師の力量の差によるものでもあろうが，それを見越して依頼する司法側の要因も影響していると思われる。また，今後増加が予想される精神鑑定業務に本県の現状で対応できるか否かを予測するために行った質問では，「引き受けることが可能」とする意見が多く，この回答をみる限りにおいては，本県では年間に最低でも33件，最大で54件，あるいはそれ以上の精神鑑定に対処できる計算となる(図3)。われわれは，本県の精神鑑定の総件数については正確には把握していないが，公的あるいはそれに類する機関で引き受けている年間の件数や，本県での医療観察法に関連する業務が年間10件程度と想定してスタートした経緯を考慮すると，この結果は，刑事訴訟法および医療観察法における精神鑑定に対して，本県では十分対処できることを示唆している。司法精神医学人材育成という観点からは，「引き受けることが可能」とする医師の積極的な姿勢を

均等に尊重できるように，経験豊かな医師らが中心となり，関係機関との連携を図り，鑑定業務を適宜，統括・采配をするようなシステムとネットワークを作ることも必要と思われる。ちなみに，「引き受けることが可能な精神鑑定の件数」の結果は，前回の調査[1]とほぼ同様の結果であり，今後増加が予想される司法精神医学領域の業務に関しては，医療観察法施行前に懸念されていた「鑑定人の確保が困難なのではないか？」といった事態が現在でも引き続き回避できていることが示されているといえる。

次に，鑑定件数を所属機関別にみた結果では，前回の結果[1]と同様に大学病院および公立病院における件数が圧倒的に多く，本県では精神鑑定の業務は公的機関あるいはそれに類する機関に依存していることが明らかであった。特に，大学病院では，本鑑定の件数が多かった。これは，本鑑定が身体的および心理的な検査を実施する必要があるため，検査設備の整った大学病院がその役割を担っていることを反映していると思われる。

ところで，結果の項でも示したが，大学病院および公立病院に精神鑑定が集中している要因と思われる意見が，医院・クリニックの医師から出ている。すなわち，「司法精神鑑定は，面接および鑑定書作成にかなり時間を要するために，診療時間を割いて鑑定面接に出向く時間的余裕がなく，報酬面から考えても鑑定を引き受ける動機づけとして乏しい」といった意見である。これは，精神科医院・クリニックに比べるとマンパワーが豊富な公的機関あるいはそれに類する機関に精神鑑定が集中する要因を象徴する意見であると考えられる。「報酬」に関する意見は，その他の医師からも「時間的な制約が大きいため，それに見合うことが望ましい」との意見も出ており，日常の診療の合間をぬって行われる業務であることや，起訴前鑑定であった事例(被疑者)が，起訴され被告人となり，裁判という場で責任能力が争われることになった際の鑑定人の労力を考えると，鑑定料が労力に見合ったものであるべきであろう。特に，今後導入される裁判員制度が適用されるような事例の精神鑑定を担当した医師は，裁判員らが適切に判断するための工夫が求められることになる[9]ため，これまでの公判での労力に比べ相当な負担が強いられることが予想され，報酬に関する批判的意見は増加する可能性がある。しかし，この問題を「教育」の観点からみると，精神鑑定を引き受けることの阻害要因が，「時間がない」，「報酬が低い」といったものだけであれば，仮に本県における司法精神医学教育システムが確立されたとしても，その運用は空回りしてしまうことが予見される。

したがって，鑑定人となった医師の診療行為の代行を他の医師が請け負うとか，報酬を増額するといったようなことが不可能と思われる現状においては，時間的制約や報酬を度外視し，司法精神医学領域に興味を持つことができるような意識改革も視野に入れた魅力ある教育システムの確立が必要となる。そのためには，教育機関でもある大学病院に所属するわれわれが，積極的に精神鑑定を引き受け，鑑定医の養成のみならず，医師になる前からの教育，つまり卒前からの医学部生に対する包括的教育システムを確立していく必要があると考える。

具体的に示すと，精神鑑定医の養成に際しては，前回と今回の調査結果から，経験を積んだ医師の鑑定助手としての業務を担当させることから導入し，実際に精神鑑定の依頼があった場合には，事前に鑑定内容を上級医師らが可能な限り吟味し，鑑定人候補者の中から経験と力量を考慮したうえで鑑定人を決定していくことが好ましいと考える。ところで，第103回日本精神神経学会総会の教育講演において，中谷[6]が「簡易鑑定は責任が重く，判断に迷うような事例に関しては，積極的に本鑑定まで行う必要がある旨を記載すべきである」と述べていたが，われわれの調査結果では，初めて担当した精神鑑定は，簡易鑑定が圧倒的に多かった。このことは，依頼される精神鑑定は簡易鑑定が多いということも関係しているのであろうが，中谷の指摘[6]からすると好ましくない状況であるといえる。とはいえ，これまでのわれわれの経験からは，本鑑定は起訴され裁判になった場合に，司法側から証人尋問の依頼がくる可能性の高い精神鑑定である。したがって，中谷の指摘したように，「簡易鑑定は司法側に都合良く利用される可能性のある責任の重い鑑定」でもあるかも

しれないが，本県の現状からは，初めて担当する精神鑑定の種類は，簡易鑑定および本鑑定といった鑑定種別にこだわらず，いずれの精神鑑定を引き受けるにせよ，事前に可能な限り吟味したうえで，精神鑑定の“初心者”に依頼するか否かを判断していくしかないであろうと思われる。そして，中谷[6]が指摘しているように，簡易鑑定の段階で判断に迷うような事例に関しては，積極的に本鑑定まで行う必要がある旨を記載すべきであろう。

一方，卒前教育は，この分野への動機づけに大きく影響を与えることが予想されるため，精神科カリキュラムの見直し，教員の講義形式や臨床実習の進め方などを再検討し，さらにすでに実践していることではあるが，大学病院に勤務する医師が，これまで以上に積極的に精神鑑定業務を引き受け，卒前教育に反映できる鑑定事例の集積を図っていく必要があると思われる。そして，これらが実践され魅力ある教育システムが確立されると，精神鑑定に対する動機づけを「時間的制約」や「報酬」に帰結させるような事態は解消されると思われる。

次に，精神鑑定の結果についてであるが，「有責」と判断されている事例に比べ，「心神喪失」あるいは「心神耗弱」といった結論に至っている事例が多いことから，司法関係者からの精神鑑定の要請は適切なものであることが示唆される。しかし，その後の被疑者の処遇に関しては，鑑定人が「知らない」とする回答が全体の半数近くに及んでいること，被告人の判決にどの程度鑑定人の意見が反映されたのか不明であること，さらに，自由意見において，「検察側から鑑定人へのフィードバックがない」といった指摘がなされているようなことは，司法精神医学教育という点からは好ましくない事態である。なぜなら，鑑定人自身が精神鑑定の結果を知ることは，自ら行った精神鑑定が司法判断にどの程度貢献できたものであったのかを知るうえで重要であり，検察官などの司法側からフィードバックを受けることは，鑑定医としての技能向上に繋がるからである。マスコミで報道されるような重大犯罪・触法行為の場合は，テレビや新聞などで，その後の被告人・被疑者の処遇を知る機会があるわけであるが，マスコミが報道しない犯罪・触法行為に関しては，司法側からの情報提供に依存するしかなく，司法側のフィードバックがなければ鑑定人はその後の処遇を知る術がない。したがって，精神鑑定の技術向上のためにも，今後は司法関係者との意見交換の場として，鹿児島県司法精神医学研究会(仮称)を発足させる必要があると思われる。

また，司法人材育成のシステムおよびネットワーク構築に関する具体的方策として，本県でも導入が可能と思われるものを自由意見の中から抽出すると，「事例検討会や研修会の開催」，「司法精神医学教育の中核を担う施設の設置」があげられる。中でも「事例検討会や研修会の開催」を希望する意見は非常に多かった。これは，調査に回答した医師らが，半ば独学に近い形で行っている精神鑑定業務への不安と，司法精神医療が立法化されたことに対する責任の重大さを感じていることを反映しているものと思われた。

その他に「研修会の開催は，大学病院主導で行ってほしい」との自由意見もみられた。これらの意見を実現する方向で検討すると，司法精神医学教育の中核を担う施設・部署の設置は必至であり，それは卒前からの教育をも担っている大学病院に設置するのが好ましいと思われた。ちなみに，その中核を担う機関の呼称としては，前回の調査[1]では「司法精神医学教育センター」，今回は「精神保健ネットワーク」という名称も提案されているが，呼称については，精神鑑定業務が一極集中を煽るような事態にならないようなものが望ましいと考えている。

以上を総括すると，精神鑑定をはじめとする司法精神医学領域の業務に豊富な経験を持つ医師らが中心となり，司法精神医学教育の中核的施設・部署を設置し，関係機関とのスムーズな連携を図り，精神鑑定業務の統括およびデータの集積を行っていくという方策がより現実的かつ合理的である。これは，今回の調査において，本県で対応できる精神鑑定件数が，年間最低でも33件，最大で54件，あるいはそれ以上といった結果が得られているように，本県には司法精神医学に興味を示す医師が比較的多いことからも極めて実現可能性の高い計画と考えている。今後は，上記方策