Eur Arch Psychiatry Clin Neurosci (1991) 241:139–144

European Archives of Psychiatry and Clinical Neuroscience

Brain Gamma-aminobutyrate Transaminase and Monoamine Oxidase Activities in Suicide Victims

Fathi Sherif[1], Jan Marcusson[2], and Lars Oreland[1]

[1]Department of Medical Pharmacology, Uppsala University, BMC, Box 593, S-751 24 Uppsala, Sweden
[2]Department of Geriatric Medicine, Linköping University, S-582 46 Linköping, Sweden

Received April 15, 1991

Summary. The activity of gamma-aminobutyrate aminotransferase (GABA-T) and monoamine oxidase (MAO-A and -B) was measured in 42 postmortem human brains. Three brain regions (frontal cortex, cingulate cortex and hypothalamus) from 23 controls without known neurological or psychiatric disorder and from 19 suicide victims were analysed. The suicide victims were classified according to the use of violent and non-violent methods and to the presence or absence of a known history of depressive disorder. No difference was found between the series of suicide victims and the control subjects with regard to GABA-T activity. Carbon monoxide poisoning and death by drug overdose, however, were found to reduce the activity. The MAO-B activity did not differ between the groups. With MAO-A, however, a significant elevation ($t = 2.01$; $P < 0.05$) was found in the hypothalamic region of the suicide victims. The difference seemed to be confined to the subgroup of suicides with a record of depressive disorder.

Key words: Aminobutyrate aminotransferase – Monoamine oxidase – Suicide – Depression – Postmortem brain

Introduction

There have been many reports of a disturbed function of brain serotonergic mechanisms in patients with suicidal behaviour. Thus, the levels of serotonin (5-HT) and/or its metabolite 5-hydroxyindoleacetic acid (5-HIAA) have, in several studies, been found to be reduced in brain tissue and/or cerebrospinal fluid (CSF) from both depressed and non-depressed patients (Shaw et al. 1967; Bourne et al. 1968; Pare et al. 1969; Lloyd et al. 1974; Beskow et al. 1976; Åsberg et al. 1976; Träskman et al. 1981; Montgomery and Montgomery 1982; van Praag 1983; Åsberg 1986; Roy et al. 1987). Moreover, in the subgroup of suicidal patients with low levels of 5-HIAA in the CSF, the attempts have been by more active and violent methods than in patients with normal or high levels (Åsberg et al. 1976; Träskman et al. 1981). It should, however, be noted that there have also been studies showing no change or even increased CSF levels of serotonin or 5-HIAA in subjects who had attempted suicide (Kauert et al. 1984; Stanley et al. 1986; Arato et al. 1987). The results from the studies on CSF are paralleled by findings of low monoamine oxidase activity (MAO; E.C. 1.4.3.4) in platelets in patients with suicidal behaviour, probably confined to the subgroup using violent methods (Buchsbaum et al. 1977; Gottfries et al. 1980). In several studies, this enzyme activity has been found to be correlated with CSF levels of 5-HIAA also in controls, and the hypothesis has been put forward that the platelet MAO activity is a genetic marker for the "size" or the functional capacity of the central serotonin system (Oreland and Shaskan 1983; Oreland 1991). So far, it has not been possible to demonstrate directly a correlation between platelet and brain MAO, but there is evidence for a correlation both between the activity of the A- and of the B-form of the enzyme and the density of the serotonergic innervation in various regions of the rat brain (Sakurai et al. 1990). Serotonin has a much higher affinity for MAO-A than for MAO-B, but, since there is a high proportion of MAO-B within the serotonergic nerve terminals, there seems to be a considerable proportion of serotonin also metabolised through the catalytic action of MAO-B (Fagervall and Ross 1986). For this reason, and since it can not be foreseen whether a possible connection between brain serotonergic turnover and brain tissue MAO might be based on the serotonin deamination rate catalysed by the enzyme(s) or on its linkage as a genetic marker to the density of serotonergic nerve terminals, both MAO-A and -B were considered to be of equal interest in the present study material of postmortem suicidal brains.

MAO activity in brains from suicide victims has previously been studied in a limited number of reports. Grote et al. (1974), using a fluorometric method with kynuramine as substrate (mainly estimating the A-form), found no difference, either between depressed suicides or alcoholic suicides and controls in a variety of brain regions; however, there were few cases with a large age variation.

Offprint requests to: L. Oreland

Gottfries and co-workers (1975), estimating preferentially the B-form of the enzyme, found reduced activity in patients where the suicide was associated with alcoholism. Lower brain MAO-A activity in alcoholics in comparison with controls was later found by Oreland et al. (1983). The reduced activity was, however, restricted to the hypothalamus and caudatus, while, in agreement with the results of Major et al. (1985), normal activity was found in the cortex gyrus cinguli and hippocampus. The low activity seemed to be confined to MAO-A and to MAO-B; however, there was some difficulty in evaluating MAO-B, because of the profound effect of age as well as of neuro-degenerative processes on this enzyme form. In a study on frontal cortices from violent suicides, without concomitant alcoholism, Mann and Stanley (1984) found no difference between controls, either in MAO-A or -B activity.

GABA-transaminase (GABA-T) (4-aminobutyrate: 2-oxoglutarate aminotransferase – E.C. 2.6.1.19) is mainly responsible for the catabolism of gamma-aminobutyric acid (GABA) and therefore its study may be of interest in connection with a variety of disorders. No such studies have, however, so far been reported. A possible change in GABA levels in one or more brain regions has been implicated in the aetiology of neuro-psychiatric disorders, such as epilepsy, Huntington's chorea, Parkinson's disease, tardive dyskinesia and schizophrenia (Schwarcz et al. 1977; Gold et al. 1980; Fibiger and Lloyd 1984; Petty and Sherman 1984; Perry et al. 1989; Meldrum 1989). The reported studies of GABA levels or GABA receptors in connection with suicide or depressive states have, however, been negative (Cross et al. 1988; Korpi et al. 1988). Experimental studies nevertheless strongly indicate that endogenous GABA is of importance for the regulation of anxiety (Sanger 1985; Shekhar et al. 1990), which is a symptom closely associated with suicidal behaviour (Goldney 1981).

Materials and Methods

Controls and Suicides

The study was of brains from 23 control subjects (19 men, 4 women), age range 16–75 years (49.44 ± 3.85 years, mean ± SEM), with no sign of mental disturbance or cognitive impairment and no other organic neurological disease or psychiatric illness necessitating continuous drug treatment. The cases were collected to match the suicide series as closely as possible with regard to age, gender and time to postmortem. Causes of death were ischaemic heart disease (IHD), drowning, car accident, or avalanche victims and one was killed by accidental carbon monoxide poisoning in a house fire.

The suicide series consisted of brains from 19 (13 men, 6 women), age range 22–75 years (42.89 ± 4.64 years, mean ± SEM) confirmed suicide victims. Nine of them had used violent acts (hanging and shooting), 5 had taken an overdose of benzodiazepines, neuroleptics or analgesics alone or in combination and 5 had committed suicide by means of carbon monoxide poisoning. Seven of the suicide victims had a clear history of depression before death, while there were no records of depressive illness in 12. Cases with alcoholism and drug abuse were excluded on the basis of reports to the medical examiner by their physician and relatives. The control and suicide series are further described in Table 1.

Table 1. Main characteristics of control subjects and suicide victims

Data	Control subjects	Suicide victims
n	23	19
Sex (M/F)	19/4	13/6
Age (years)	49.44 ± 3.86 (16–75)	42.90 ± 4.64 (22–75)
Postmortem delay (hours)	42.57 ± 3.27 (19–72)	49.42 ± 3.48 (24–72)
Brain weight (g)	1521.17 ± 30.14 (1271–1801)	1503.42 ± 29.26 (1320–1754)
Storage time (months)	13.91 ± 1.09 (5–20)	13.37 ± 1.20 (5–22)

Values are expressed as means ± SEM, range is shown in parentheses
All brain samples were assayed in 1 week and each brain region was assayed in quadruplicate for MAO and in duplicate for GABA-T
There were no statistically significant differences between the groups (unpaired *t*-test)

Brain Dissections and Storage

The brain specimens were collected at the Department of Forensic Medicine, University of Umeå, Umeå, Sweden. Both control and suicide samples were collected over the same period of time (all tissues were collected between 1989 and 1990). There were no differences between the two groups with regard to postmortem time before dissection and freezing or storage time before analysis (Table 1). Tissues were dissected at autopsy from frontal cortex, cingulate cortex and hypothalamus and subsequently stored at −80°C until neurochemical analysis. Storage of the tissue or homogenate at −80°C for at least 1 year does not significantly alter enzyme activity (Fowler et al. 1980; Sherif et al. 1991).

Biochemical Methods

The brain tissue was homogenised by six strokes at 600 rpm in 0.32 M of ice-cold sucrose (1:9 w/v) in a Potter-Elvehjem glass/Teflon pestle system.

GABA-T Assay

GABA-T activity was assayed in the homogenates using the radiochemical method of White (1979) as modified by Sherif et al. (1991), in which (^{14}C)-GABA is converted to (^{14}C)-succinic semialdehyde. Homogenate aliquots (25 µl) were added to 25 µl of 0.68 mM alpha-ketoglutarate, 25 µl of incubation medium (0.05 mM EDTA, 0.25 mM dithiothreitol, 0.1 mM pyridoxal phosphate, 0.05 mM disodium phosphate, pH 8.4) and 25 µl of ^{14}C-GABA, 2 mM (specific radioactivity = 0.233 µCi per mmol, NEN Research Products, Boston, Mass). Incubation was carried out at 37°C for 30 min. Blanks were obtained by omission of alpha-ketoglutarate. The assay was stopped on ice, 30 µl of 1 M HCl added and the mixture passed through an ion-exchange column (Biorad AG 50W-X8 resin, Bio-Rad Laboratories, Richmond, USA). The eluate was counted with 15 ml of scintillation liquid (Ready protein, Beckman, Ireland) in a Packard liquid scintillation counter. All assays were performed in duplicate.

MAO Assay

MAO-A and -B activities were assayed radiochemically by a conventional method (Eckert et al. 1980) with ^{14}C-5-hydroxytryptamine (5-HT) and ^{14}C-2-phenylethylamine hydrochloride (PEA) (NEN Research Products, Boston, Mass) respectively, as sub-

strates at a concentration of 0.1 mM for 5-HT and 0.05 mM for PEA. Radioactivity was determined by liquid scintillation counting using Beckmann scintillation fluid. All assays were performed in quadruplicate.

Samples from suicide victims and matched controls were paired in the same assay run from the three brain regions (7 suicide victims and 7 control subjects from the three regions at the same run). This design was adopted to minimize the possible influence of technical assay factors.

The reproducibility of the assay was tested by estimating homogenate aliquots from a control human brain several times. The intra-assay coefficients of variation of the assay for GABA-T was found to be 5% (similar to Bolton et al. 1989) and for MAO less than 5%.

Protein concentration was estimated according to Lowry et al. (1951) as modified by Markwell et al. (1978) using bovine serum albumin as a standard.

Results

The main characteristics of the suicide victims and control subjects are shown in Table 1. Mean age, postmortem time (the time between death and freezing of the dissected tissues at −80°C), brain weight and tissue storage time (the time from storage of the dissected tissues to the assay in months) did not differ significantly between suicides and controls.

Effect of Age and Postmortem Delay on GABA-T and MAO Activities

The correlations between age and activities of GABA-T, MAO-A and -B in the frontal cortex, cingulate cortex and hypothalamus were calculated for the control group. There was a significant positive correlation between age and MAO-B activity in both cortical regions. No significant correlations were found between age and MAO-A or GABA-T activities in any of the brain regions studied. There was, however, a significant correlation between age and postmortem time in the control group ($r = -0.51$; $P < 0.01$; $n = 23$). For that reason, multiple regression analyses were performed on the enzyme activities versus age and postmortem time. However, although the consideration of the postmortem time of some cases increased the correlation coefficients, still no statistically significant influence of age was found on GABA-T or MAO-A activities (data not shown). When the effect of postmortem time on the enzyme activities was calculated by simple regression, no significant correlations were found, except for MAO-B in the frontal cortex ($r = -0.42$; $P < 0.05$; $n = 23$). Since MAO-B activity increases with age and there was a correlation between age and postmortem time in the present material, the influence of the postmortem time on MAO-B activity in the cortex was investigated by multiple regression analysis. In this way, a significant positive correlation was found ($r = 0.52$; $P < 0.05$; $n = 23$). In summary, MAO-B increased with age in the cortical regions, and, except for a positive correlation between MAO-B in the frontal cortex and postmortem, neither age nor postmortem time had any influence on GABA-T or MAO-A activities.

Table 2. Activities of GABA-T and MAO-(A and B) in the brain regions of control subjects and suicide victims

Subjects	Hypothalamus	Frontal cortex	Cingulate cortex
GABA-T			
Controls (23)	0.912 ± 0.021	0.928 ± 0.022	0.750 ± 0.018
Suicides (19)	0.913 ± 0.020	0.897 ± 0.027	0.725 ± 0.019
MAO-A			
Controls (22)	0.420 ± 0.015	0.235 ± 0.007	0.279 ± 0.008
Suicides (19)	0.466 ± 0.018[a]	0.229 ± 0.010	0.269 ± 0.010
MAO-B			
Controls (23)	2.004 ± 0.018	0.835 ± 0.050	0.991 ± 0.056
Suicides (19)	2.062 ± 0.130	0.776 ± 0.067	0.882 ± 0.073

Activities of GABA-T and MAO (-A and -B) are given as means ± SEM in nmol/min per mg of protein for the number of subjects shown in parentheses

[a] Significant difference is denoted by $P < 0.05$ ($t = 2.01$; unpaired t-test)

Comparison Between Suicides and Controls

Table 2 shows the activities of GABA-T and MAO-A and -B in the three brain regions of controls and suicides. No difference was found in GABA-T or MAO-B activity between the groups in any of the brain regions studied. Not did MAO-A activity differ significantly between the two groups in the cortical regions. In the hypothalamus, however, there was an increase in the suicide group ($t = 2.01$; $P < 0.05$; $n = 19$).

Comparison Between Suicides With and Without Clinical Signs of a Depressive Disorder

When the suicides were divided into subgroups with and without records of clinical signs of a depressive disorder, no significant differences were found between controls, matched for age and postmortem time, and either subgroup of suicides with regard to GABA-T or MAO-B activities. The MAO-A activity in the hypothalamus, however, was found to be significantly higher only in the suicide subgroup with records of a depressive disorder [0.490 ± 0.031 nmol/protein mg/min for depressed suicides and 0.386 ± 0.033 nmol/protein mg/min for matched controls (Mean ± SEM); $t = 1.97$; $P < 0.05$; $n = 7$].

The Effects of Carbon Monoxide and Drug Overdose

In the series of suicides, 5 subjects and, among the controls, 1 subject had died from carbon monoxide poisoning. The enzyme activities of those 6 subjects were compared with those of 6 controls, matched for age and postmortem time. The results indicate that there was a significant reduction (13% of control value; $t = 3.73$; $P < 0.01$) in the frontal cortices of the carbon monoxide group with regard to GABA-T activity. When the 5 suicide victims, who had died from a drug overdose, were compared with 5 control subjects, matched for age and postmortem time, a reduction was found in GABA-T activity in the frontal cortices (18% of control value; $t = 2.66$; $P < 0.05$).

Comparison Between Controls and Suicides Using Violent or Non-Violent Methods

The 9 suicide victims who had used violent methods (e.g. hanging or shooting), did not differ from 9 controls, matched for age and postmortem time, in any of the three enzyme activities investigated. When the enzyme activities of the suicides, using non-violent methods (5 carbon monoxide and 5 drug overdose), were compared with those of 10 controls, matched for age and postmortem time, no difference was found in GABA-T or MAO-(A and B) activities between the groups in any of the brain regions studied (data not shown).

Correlation Between GABA-T and MAO Activities

No correlation was found in the control group between GABA-T and MAO-A or -B activities in any of the brain regions investigated. MAO-A and -B activities, however, showed high correlations in all three regions (correlation coefficients ranging from 0.60 to 0.76).

Discussion

The major findings in the present study are that neither GABA-T nor MAO-B activities were changed in brain tissues (frontal cortex, cingulate cortex and hypothalamus) from subjects who had committed suicide in comparison with controls. With regard to MAO-A activity, however, a higher activity was found in the hypothalamus region in the brains of the suicide victims. This difference was most marked for the subgroup of suicides with a record of depressive disorder.

The present data on brain GABA-T activity, estimated on a clinical material, is the first, to our knowledge, ever reported. The finding of unchanged GABA-T activity in brain tissue from subjects who had committed suicide is in line with the reports about unchanged activity of the GABA-synthetizing enzyme glutamic acid decarboxylase (GAD) (Cheetham et al. 1988) as is the finding of unchanged levels of GABA in brains from such subjects (Korpi et al. 1988). In depressed patients, however, GABA levels, both in plasma (Petty et al. 1987) and CSF (Gold et al. 1980; Gerner and Hare 1981), have been reported to be reduced. There have been no reports about levels of GABA in the plasma or CSF in suicidal patients.

The suicide group was subdivided in various ways. When the subjects were classified according to the absence or presence of records of depressive disorder, 7 out of the 19 subjects were assigned to the latter group. Such a proportion (37%) is in good agreement with the general figure of depressive disorders in connection with suicide in Sweden (Weeke 1979). No differences in GABA-T activities were, however, found between those two groups. Another way of subdivison was classification of those using active and passive methods, respectively. Previously, mainly the group using active methods has been shown to differ from controls with regard to levels of the serotonin metabolite 5-hydroxyindoleacetic acid in the cerebrospinal fluid (Träskman et al. 1981; Brown et al. 1982; Linnoila et al. 1983). However, this way of subclassification also did not result in any difference in GABA-T activity.

The present finding of a significantly elevated MAO-A activity in the hypothalamus region in brains from depressed suicides is at variance with the results of Grote et al. (1974). The present material, however, is considerably larger and the MAO-A activity estimated with a more reliable technique, which might explain the considerably greater variation within the material in the previous study (SD 37% of the mean activity) in comparison with ours (SD 17% of the mean activity). The result is unlikely to be caused by age, gender, postmortem delay or tissue storage, since suicides and controls were well matched for these variables. For some unknown reason, the activities of MAO-A in the hypothalami of the matched control groups for the depressed and non-depressed suicides differed, which is why caution is necessary in the interpretation of the results. It is of interest that MAO-B, which is usually correlated with MAO-A (present results and Fowler et al. 1980), was not changed. Although the literature is not very consistent on this point (see Åsberg et al. 1987 for review), there are a number of reports with reduced levels of serotonin in suicide cases, particularly in the hypothalamus region (Korpi et al. 1983; Rehavi et al. 1985; Korpi et al. 1986). Previous findings of reduced imipramine and increased serotonin (S-2) receptor binding in brain cortex tissue from suicide victims also support the notion of low brain levels of serotonin, at least in this region, in such subjects (Stanley et al. 1982; Stanley and Mann 1983). Serotonin is mainly a substrate for the A-form of MAO (Fagervall and Ross 1986) and it can be speculated that a high MAO-A activity might have contributed to the low levels of serotonin.

Although the relationship between the activity of MAO in brain and function of serotonergic system is likely to be complex (Oreland et al. 1984), a positive correlation between MAO activities and serotonin turnover has been reported in control brains (Adolfsson et al. 1978) and between various regions of the rat brain (Sakurai et al. 1990). Such a relationship would implicate a high turnover of serotonin in the hypothalamus region of the depressed suicide cases. It is, however, possible that such a correlation only reflects basic (normal) conditions, and that a depressive disorder disturbs the correlation. Previously, it has been found that the correlation between platelet MAO activity and CSF levels of 5-HIAA only prevails in control cases and could not be found in patients with depressive disorders (Oreland et al. 1981).

Acknowledgements. The skillful technical assistance of Miss Ulla Thornström is gratefully acknowledged.

References

Adolfsson R, Gottfries CG, Oreland L, Roos BE, Wiberg Å, Winblad B (1978) Monoamine oxidase activity and serotoninergic turnover in human brain. Prog Neuropsychopharmacol Biol Psychiatry 2:225–230

Arato M, Tekes K, Tothfalusi L, Magyar K, Palkovits M, Demeter E, Falus A (1987) Serotonergic split brain and suicide. Psychiatry Res 21:355–356

Åsberg M (1986) Biochemical aspects of suicide. Clin Neuropharmacol 9:374–376

Åsberg M, Schalling D, Träskman L, Wägner A (1987) Psychobiology of suicide, impulsivity and related phenomena. In: Meltzer HY, Coyle JT, Kopin IJ, Bunney WE, Davis KL, Schuster CR, Shader RI, Simpson GM (eds) Psychopharmacology, the third generation of progress. Raven Press, New York, pp 655–668

Åsberg M, Thorén P, Träskman L, Bertilsson L, Ringberger V (1976) "Serotonin depression" A biochemical subgroup within the affective disorders? Science 191:478–480

Beskow J, Gottfries CG, Roos BE, Winblad B (1976) Determination of monoamine metabolites in the human brain: postmortem studies in a group of suicides and in a control group. Acta Psychiatr Scand 53:7–20

Bolton JB, Rimmer E, Williams J, Richens A (1989) The effect of vigabatrin on brain and platelet GABA-transaminase activities. Br J Clin Pharmacol 27:35S–42S

Bourne HR, Bunney WE, Colburn RW, Davis JM, Davis JN, Shaw DM, Coppen AJ (1968) Noradrenaline, 5-hydroxytryptamine, and 5-hydroxyindoleacetic acid in hindbrains of suicidal patients. Lancet II:805–808

Brown GL, Ebert MH, Goyer PF, Jimerson DC, Klein WJ, Bunney WE, Goodwin FK (1982) Aggression, suicide and serotonin: relationships to CSF amine metabolites. Am J Psychiatry 139:741–746

Buchsbaum MS, Haier RJ, Murphy DL (1977) Suicide attempts, platelet monoamine oxidase and the average evoked response. Acta Psychiatr Scand 56:69–79

Cheetham SC, Crompton MR, Katona CLE, Parker SJ, Horton RW (1988) Brain $GABA_A$/benzodiazepine binding sites and glutamic acid decarboxylase activity in depressed suicide victims. Brain Res 460:114–123

Cross JA, Cheetham SC, Crompton MR, Katona CLE, Horton RW (1988) Brain $GABA_B$ binding sites in depressed suicide victims. Psychiatry Res 26:119–129

Eckert B, Gottfries CG, Knorring L von, Oreland L, Wiberg Å, Winblad B (1980) Brain and platelet monoamine oxidase in mental disorders 1. Schizophrenics and cycloid psychotics. Prog Neuropsychopharmacol Biol Psychiatry 4:57–68

Fagervall I, Ross SB (1986) A and B forms of monoamine oxidase within the monoaminergic neurons of the rat brain. J Neurochem 47:569–576

Fibiger HC, Lloyd KG (1984) Neurobiological substrates of tardive dyskinesia: the GABA hypothesis. Trends Neurosci 7: 642–464

Fowler CJ, Wiberg Å, Oreland L, Marcusson J, Winblad B (1980) The effect of age on the activity and molecular properties of human brain monoamine oxidase. J Neural Transm 49:1–20

Gerner RH, Hare TA (1981) CSF GABA in normal subjects and patients with depression, schizophrenia, mania, and anorexia nervosa. Am J Psychiatry 138:1098–1101

Gold BI, Bowers MB, Roth RH, Sweeney DW (1980) GABA levels in CSF of patiens with psychiatric disorders. Am J Psychiatry 173:362–364

Goldney RD (1981) Attempted suicide in young women: correlates of lethality. Br J Psychiatry 139:382–390

Gottfries CG, Oreland L, Wiberg Å, Winblad B (1975) Lowered monoamine oxidase activity in brains from alcoholic suicides. J Neurochem 25:667–673

Gottfries CG, Knorring L von, Oreland L (1980) Platelet monoamine oxidase activity in mental disorders – 2. Affective psychoses and suicidal behaviour. Prog Neuropsychopharmacol Biol Psychiatry 4:185–192

Grote SS, Moses SG, Robins E, Hudgens RW, Croninger AB (1974) A study of selected catecholamine metabolising enzymes: a comparison of depressive suicides and alcoholic suicides with controls. J Neurochem 23:791–802

Kauert G, Gilg TH, Eisenmenger W, Spann W (1984) Postmortem biogenic amines in CSF of suicides and controls. Collegium International Neuro-Psychopharmacologicum. 14th C.I.N.P., congress, Florence, Italy, June 19–23, 1984, pp 393

Korpi ER, Goodman SI, Wyatt RJ, Kleinman JE (1983) Concentrations of serotonin and 5-hydroxyindoleacetic acid in different postmortem brain areas of chronic schizophrenic patients and suicide victims. J Neurochem 41:S103

Korpi ER, Kleinman JE, Goodman SI, Phillips I, DeLisi LE, Linnoila M, Wyatt RJ (1986) Serotonin and 5-hydroxyindoleacetic acid in brains of suicide victims. Arch Gen Psychiatry 43:594–600

Korpi ER, Kleinman JE, Wyatt RJ (1988) GABA concentrations in forebrain areas of suicide victims. Biol Psychiatry 23:109–114

Linnoila M, Virkkunen M, Scheinin M, Nuutila A, Rimon R, Goodwin FK (1983) Low cerebrospinal fluid 5-hydroxyindoleacetic acid concentration differentiates impulsive from nonimpulsive violent behaviour. Life Sci 33:2609–2614

Lloyd KG, Farley IJ, Deck JHN, Hornykiewicz O (1974) Serotonin and 5-hydroxyindoleacetic acid in discrete areas of the brainstem of suicide victims and control patients. Adv Biochem Psychopharmacol 11:387–397

Lowry OH, Rosebrough NJ, Farr AL, Randall RJ (1951) Protein measurement with the folin phenol reagent. J Biol Chem 193:265–275

Major LF, Hawley RJ, Saini N, Garrick NA, Murphy DL (1985) Brain and liver monoamine oxidase type A and type B activity in alcoholics and controls. Alcoholism: Clin Exp Res 9:6–9

Mann JJ, Stanley M (1984) Postmortem monoamine oxidase enzyme kinetics in the frontal cortex of suicide victims and controls. Acta Psychiatr Scand 69:135–139

Markwell MAK, Haas SM, Bieber LL, Tolbert NE (1978) A modification of the Lowry procedure to simplify protein determination in membrane and lipoprotein samples. Anal Biochem 87: 206–210

Meldrum BS (1989) GABAergic mechanisms in the pathogenesis and treatment of epilepsy. Br J Clin Pharmacol 27:3S–11S

Montgomery SA, Montgomery D (1982) Pharmacological prevention of suicidal behaviour. J Affect Disord 4:291–298

Oreland L (1991) Monoamine oxidase in neuro-psychiatric disorders. In: Yasuhara H, Parvez SH, Sandler M, Nagatsu T (eds) Monoamine oxidase, basic and clinical aspects. VSP Press, AH Zeist, Holland (in press)

Oreland L, Shaskan EG (1983) Monoamine oxidase activity as a biological marker. Trends Pharmacol Sci 4:339–341

Oreland L, Wiberg Å, Åsberg M, Träskman L, Sjöstrand L, Thorén P, Bertilsson L, Tybring G (1981) Platelet MAO activity and monoamine metabolites in cerbrospinal fluid in depressed and suicidal patients and in healthy controls. Psychiatry Res 4:21–29

Oreland L, Wiberg Å, Winblad B, Fowler CJ, Gottfries CG, Kiianmaa K (1983) The activity of monoamine oxidase-A and -B in brains from chronic alcoholics. J Neural Transm 56:73–83

Oreland L, Knorring L von, Schalling D (1984) Connections between monoamine oxidase, temperament and disease. In: Paton W, Mitchell J, Turner P (eds) Proceedings of the IUPHAR 9th International Congress of Pharmacology. Macmillan, London, pp 193–202

Pare CMB, Yeung DPH, Price K, Stacey RS (1969) 5-hydroxytryptamine, noradrenaline, and dopamine in brainstem, hypothalamus, and caudata nucleus of controls and of patients committing suicide by coal-gas poisoning. Lancet II:133–135

Perry TL, Hansen S, Jones K (1989) Schizophrenia, tardive dyskinesia, and brain GABA. Biol Psychiatry 25:200–206

Petty F, Sherman AD (1984) Plasma GABA levels in psychiatric illness. J Affect Disord 6:131–138

Petty F, Kramer G, Feldman M (1987) Is plasma GABA of pepheral origin? Biol Psychiatry 22:725–732

Praag HM van (1983) CSF 5-HIAA and suicide in non-depressed schizophrenics. Lancet II:977–978

Rehavi M, Skolnick P, Paul SM (1985) Characterization of high-affinity antidepressant binding to rat and human brain. In: Gram L, Usdin E (eds) Proceedings of the third international meeting on clinical pharmacology in psychiatry. Macmillan, London, pp 846–853

Roy A, Virkkunen M, Linnoila M (1987) Reduced central serotonin turnover in a subgroup of alcoholics? Prog Neuropsychopharmacol Biol Psychiatry 11:173–177

Sanger DJ (1985) GABA and behavioral effects of anxiolytic drugs. Life Sci 36:1503–1513

Sakurai E, Yamasaki S, Niwa H, Jossan SS, Hallman J, Oreland L (1990) Relation between serotonin and dopamine uptake rates, transmitter concentrations and monoamine oxidase (MAO) activities in various regions of the rat brain. Biogenic Amines 7:1–10

Schwarcz R, Bennett JP, Coyle JT (1977) Inhibitors of GABA metabolism: implications for Huntington's disease. Ann Neurol 2:299–303

Shaw DM, Camps FE, Eccleston EG (1967) 5-hydroxytryptamine in the hind-brain of depressive suicides. Br J Psychiatry 113: 1407–1411

Shekhar A, Hingtgen JN, DiMicco JA (1990) GABA receptors in the posterior hypothalamus regulate experimental anxiety in rats. Brain Res 512:81–88

Sherif F, Eriksson L, Oreland L (1991) GABA-transaminase activity in rat and human brain; regional, age and sex-related differences. J Neural Transm 84:95–102

Stanley M, Mann JJ (1983) Increased serotonin-2 binding sites in frontal cortex of suicide victims. Lancet I:214–216

Stanley M, Mann JJ, Cohen LS (1986) Problems and promises of post-mortem brain tissue analysis. Psychopharmacol Bull 22: 735–740

Stanley M, Virgilio J, Gershon S (1982) Tritiated imipramine binding sites are decreased in the frontal cortex of suicides. Science 216:1337–1339

Träskman L, Åsberg M, Bertilsson L, Sjöstrand L (1981) Monoamine metabolites in CSF and suicidal behaviour. Arch Gen Psychiatry 38:631–636

Weeke A (1979) Causes of death in manic-depressives. In: Schou M, Strömgren E (eds) Origin, prevention and treatment of affective disorders. Academic Press, London, pp 289–299

White HL (1979) 4-Aminobutyrate: 2-oxoglutarate aminotransferase in blood platelets. Science 205:696–698