Intern. J. Neuroscience, 1988, Vol. 38, pp. 11–20
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PARTIAL COGNITIVE-DYSMNESIC SEIZURES AS A MODEL FOR STUDYING PSYCHOSIS

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(Received February 15, 1987)

Nineteen patients were analyzed who exhibited cognitive-dysmnesic psychic partial seizures and structural damage shown by means of CT scans. It was observed that these seizures originated in the amygdala-hippocampal system, coinciding with the effects found when using electrical stimulation of the brain. An attempt is made to relate these findings to the present biochemical hypotheses of schizophrenia, the kindling effect and the genetico-maturational hypotheses. All these data seem to agree and point in the direction of the possible neurophysiological mechanisms of psychosis and of schizophrenia in particular.

Keywords: partial psychic seizures, psychosis, amygdala-hippocampal system, neurophysiology of schizophrenia

Some time ago, the possible existing relationship between epilepsy and psychosis caused great interest (Falret, 1860; Jackson, 1884; Turner, 1907). Over the past decades, a large number of studies have appeared confirming the existence of some association between these two phenomena (Slater & Beard, 1963; Gudmundsson, 1966; Flor-Henry, 1969; Kristensen & Sindrup, 1978; Perez & Trimble, 1980; Toone, Garralda & Ron, 1982; Trimble, 1982, 1986).

Psychotic type profiles can appear at three different times in epilepsy (Blumer & Benson, 1982): as an ictal condition in which there is a defined mental change associated with a particular neurophysiological substratum; as a postictal condition with confusion and psychic changes in some way similar to the psychotic states; and as an interictal manifestation, which often takes the form of short psychoses (days, weeks) of the schizophreniform type but without an underlying schizoid personality.

This interest in the search for possible relationships between epilepsy and psychosis has been basically directed at the analysis of the schizophreniform psychoses which can be associated with some epilepsies of the temporal lobe. However, many of the phenomena found in the psychic partial seizures (ILAE, 1981) could be considered to be elements of a psychotic profile: hallucinations, mnesic-cognitive changes, etc. They do not usually form a paroxystic psychosis but only elements, fragments of a paroxystic psychosis, elements which when found to be installed together in a permanent form would correspond to a psychotic profile. Among these partial psychic phenomena those which refer more directly to experiential or mental phenomena are the cognitive and dysmnesic partial psychic seizures. It could be supposed that their analysis in some ways helps in the clarification of the neurophysiological mechanisms and the systems that participate in the appearence of phenomena of a psychotic type.

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This research is a continuation of the study of psychic partial seizures which began several years ago (Ardila, 1983, 1984; Ardila et al., 1985, 1986a, 1986b, in press). We refer specifically to the cognitive and dysmnesic psychic partial seizures and their possible relationship to schizophrenic psychosis.

METHOD

Subjects

The review of approximately 4,000 case histories of epilepsy recorded in the Neurological Institute of Colombia over the past 13 years revealed the existence of 109 patients (2.7%) with psychic partial seizures. Since some patients presented several types of seizures, the number of "cases" came to 163 (Table 1). We believe that the real number must be considerably higher since these phenomena are frequently passed over by the patient and/or examiner. From these patients, those who exhibited dysmnesic and cognitive phenomena (53 cases) and who also had scans showing some type of focal structural damage (the CT scan was introduced into Colombia in 1977) were selected. Of the patients with cognitive–dysmnesic seizures, only 19 fulfilled this criterion (the others either had no scans, their scans showed no structural damage or they suffered from broad global processes such as generalized atrophy, or the scans were not available). Thus, the final sample used for the analysis was of 19 patients (11 men, 8 women; average age 29.6, range 14–48).

TABLE 1
Psychic partial seizures found in a total of 109 patients (163 "cases")

	Frequency	%
Illusions	22	13.50
Hallucinations	53	32.51
Affective	25	15.34
Dysphasic	10	6.13
Dysmnesic	29	17.80
Cognitive	24	14.72

Instruments

CT scans of 19 subjects taken at the Neurological Institute of Colombia between 1977 and 1986, using two different types of scanning techniques, were taken as basic data. Up to June 1982, scans were taken with a General Electric CT/N scanner with a 160×160 matrix and 1.0 cm cuts, and after that date, a General Electric CTT/8000 scanner with a 320×320 matrix and 0.5 cm cuts was used.

A template was prepared to facilitate the transcription of the scanned lesion in a uniform manner. It was designed to include 10 standard scanner cuts, each corresponding to a representative level of the brain, from the base to the most cortical portion.

Procedure

The lesions of the 19 patients shown on the scans were transferred to the previously prepared standard template. Subsequently, the different lesions were superimposed on a single template and, for each patient, the topography of the lesion was correlated with the content of the seizure.

RESULTS

Table 2 correlates the experiential description of the seizures studied with the patient's diagnosis. Figure 1 illustrates the topography of the lesion in the case of cognitive phenomena and Figure 2 the topography in the case of dysmnesic phenomena. It is worth noting that the border between these two types of seizure is imprecise; an episode frequently presents both dysmnesic and cognitive characteristics (this is the reason why both phenomena have been considered together in this research and are only separated in their graphic representations to give facility in visualization).

It can be observed that phenomena of a cognitive type (feeling of strangeness, changes in thought content, feeling of being somebody else, etc.) appear when the lesions are found in the hippocampus or adjacent structures: parahippocampal gyrus, uncus, amygdala, temporal pole, Sylvian fissure. The topography of the lesion is not essentially different in the case of dysmnesic type seizures; in fact, both tend to be associated and then it is particularly difficult to establish their borders.

Some of our patients presented other types of seizures in association with the cognitive-dysmnesic phenomena. The association most frequently found were the olfatory, autonomic, affective and dysphasic phenomena.

It is interesting to note that phenomena more exactly of the dysmnesic type appeared almost twice as frequently in lesions situated in the left hemisphere, while the more exactly cognitive phenomena appeared equally in both cerebral hemispheres.

DISCUSSION

Many of the phenomena present in psychic partial seizures (depersonalization, hallucinations, affective changes, etc.) are also found in functional psychiatric episodes. The interical psychiatric changes show the same range of mental states and behavioral phenomena as functional disorders in the absence of epilepsy (Fenton, 1981), although it has been suggested that some differences between the schizophreniform psychosis of epilepsy and primary schizophrenia could exist: less deterioration of personality, a greater relative frequency of visual hallucinations, a greater incidence of mystical and paranoid delusions, and absence of genetic predisposition (Hill, 1953). It has also been proposed that the psychosis associated with epilepsy would fit in more with a schizoaffective presentation than with an actual schizophrenia (Perez & Trimble, 1980; Toone, Garralda & Ron, 1982).

Halgren et al. (1978), using electrical stimulation of the brain, found that what they called mental phenomena (hallucinations, dreamy states, amnesic changes, etc.) appear with amygdala and hippocampal stimulation. Similarly, Gloor et al. (1982) found the experiential (mental) phenomena are produced with stimulation of the amygdala, the hippocampus and the parahippocampal gyrus.

TABLE 2
Cognitive-dysmnesic phenomena and scan findings in sample of patients studied

	Sex	Age	Description	Findings
37411	F	14	"I feel as if I knew what was going to happen." "When I speak to someone I sometimes feel that it is my brother speaking for me." "I feel that I have already dreamed about the things that are happening."	Multiple cortical and subcortical calcifications
40212	M	26	"As if what is happening had already happened a long time ago: as if I were remembering something." "I felt as if I were dreaming but awake."	Lesion of the uncus in the hippocampus
37640	F	14	"Feeling of strangeness."	Small calcification in the right basal frontal region
32265	M	21	"Strangeness of the environment." "Feeling of having lived the episode." "As if someone were seeing through me."	Hyperdense image in the basal middle line towards the tuberculum Sellae
34335	M	21	"Feeling of unreality." "I don't remember events or acts that took place at a given moment."	Vascular malformation in the left temporal region
31308	F	35	"Dreamy state."	Mesial sclerosis of the left hippocampus
38169	F	36	"Disconection from the environment." "She is quiet, listens, sees, but it is as if she didn't do it, didn't speak, she stands still staring at a point."	Zone of less density in the deep left temporal
11701	F	25	"Déjà-vu."	Residual meningotelial meningioma in the fronto-temporal middle fossa
13405	F	29	"Great mental confusion."	Right temporal multiform glioblastoma
15413	M	48	"Disorientation and feeling of unreality."	Right temporal oligodendroglioma
16528	M	37	"Déjà-vu." "Feeling of being hypnotized."	Hyperdense temporal lesion at the level of the Sylvian fissure
29671	M	38	"Strange thoughts." "Feeling of being another person."	Dense basal calcification in the left temporal
24669	M	17	"Depersonalization." "Déjà-vu."	Fronto-temporal lesions and in anterior hippocampus
32070	F	40	"Feeling of wanting to remember something." "I felt as if another person was going to take possession of my brain; as if I were on the TV." "I saw images in my head."	Cavernous angioma in the right temporal lobe
31136	M	35	"Feeling of repetition of facts, attitudes or words." "Feeling of lethargy . . . of absolute silence"	Astrocitoma in pole of the right temporal lobe
25032	M	36	"Déjà-vu; remembers having seen things."	Fronto-temporal anaplasic astrocytoma
24384	M	22	"Déjà-vu." "Feeling of great confusion and loss of concentration."	Left temporal multiform gliobalstoma
41148	M	43	"As if I were in a film." "Feeling that I already knew the people and places."	Left temporal lobe zone of less density
35269	F	26	"Feeling of strangeness."	Left temporal subcortical granulomatose lesion

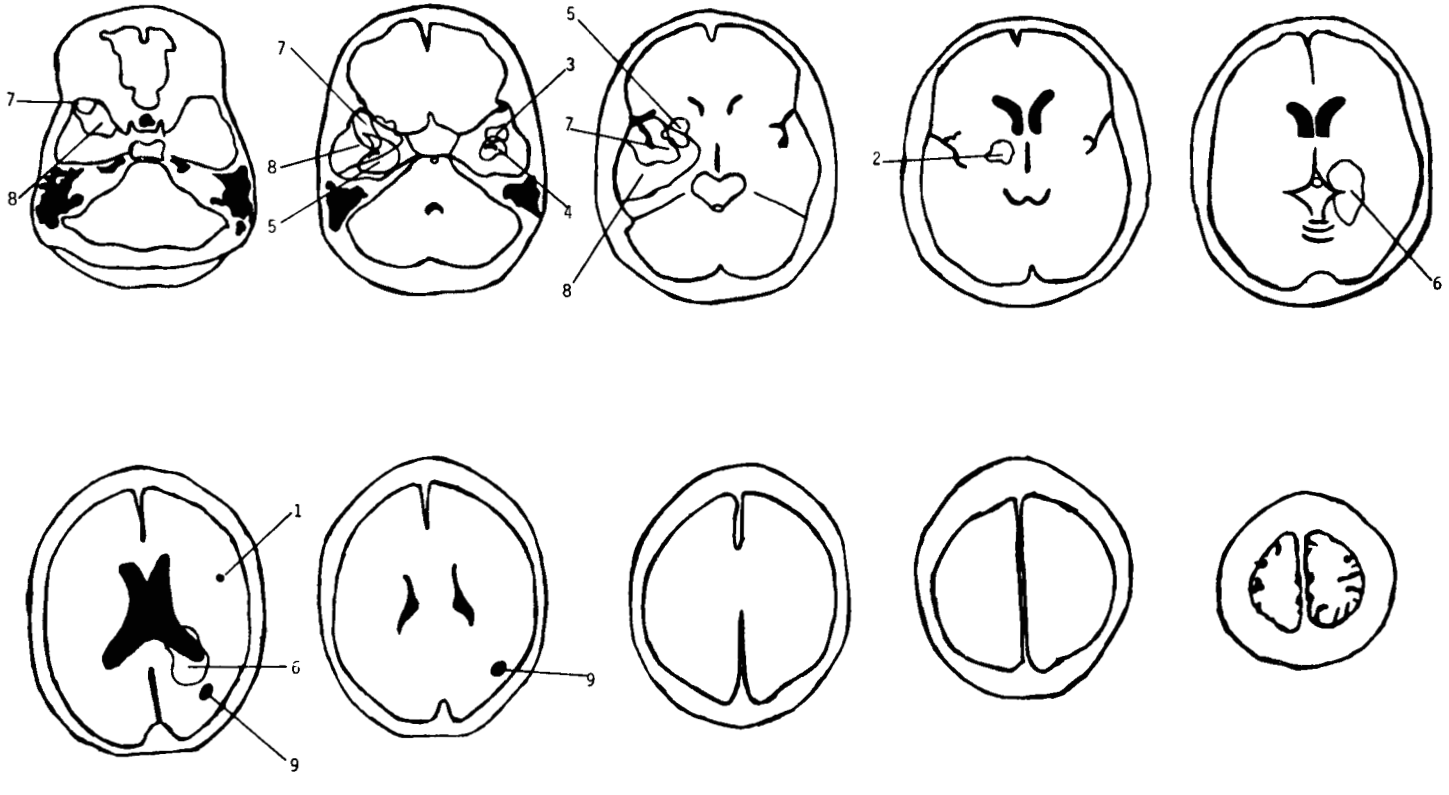

FIGURE 1 Topography of the lesions in cognitive psychic partial seizures. The associated phenomena were: (1) "I feel as if I know what is going to happen"; "when I speak, I sometimes feel that it is my brother speaking for me"; (2) "I felt as if I were dreaming but awake"; (3) "Detached from the environment"; the patient remains quiet, does not speak and on occasions replies with very long latencies; (4) "Strange thoughts, the feeling of being like another person"; (5) Depersonalization; (6) "Feeling of great confusion and loss of concentration"; (7) "Feeling of lethargy, of absolute silence"; (8) "As if I were in a film"; (9) "Feeling of strangeness."

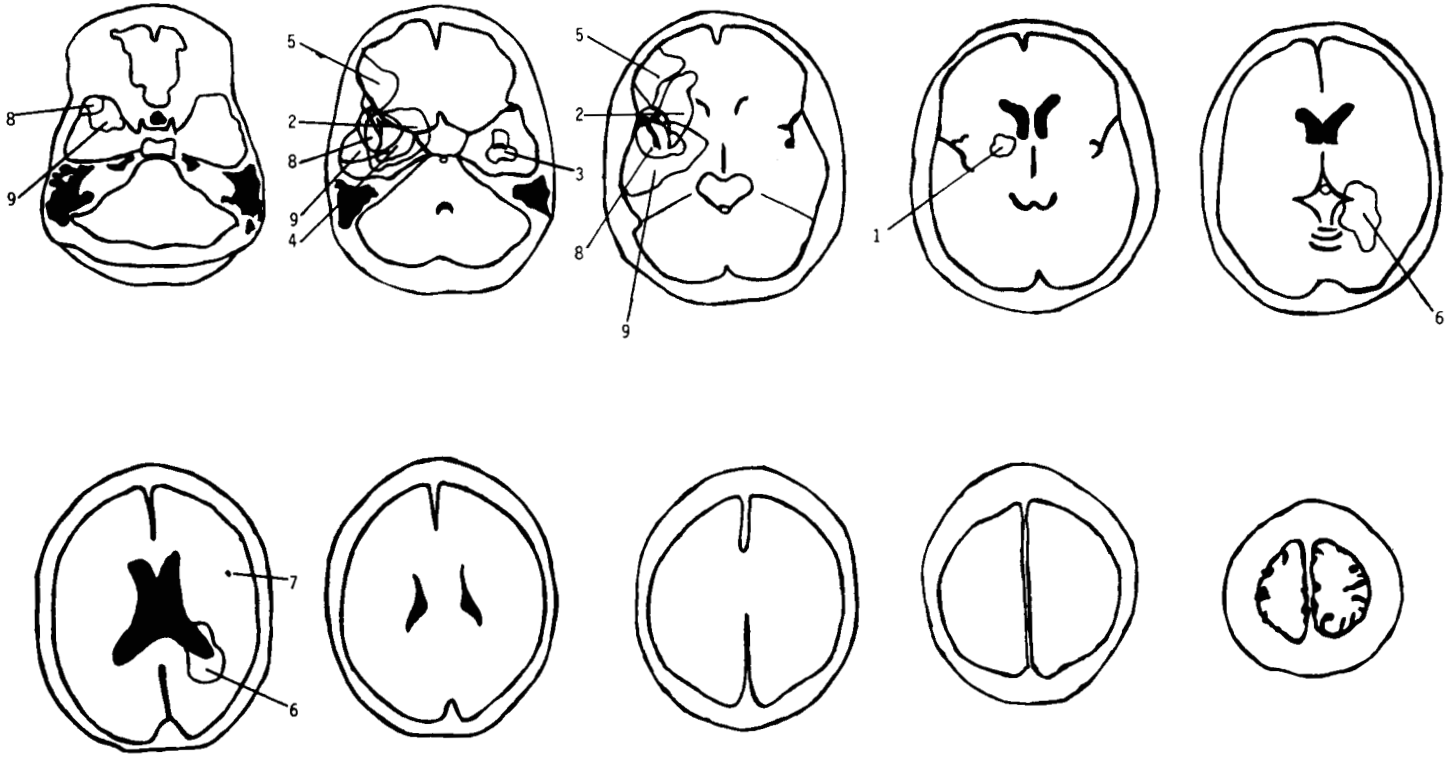

FIGURE 2 Topography of the lesions in dysmnesic psychic partial seizures. The associated phenomena were: (1) "As if what was happening had already happened a long time ago; as if I were remembering something"; (2) Déjà-vu; (3) "Forgetfulness of recent facts"; (4) Déjà-vu; (5) Déjà-vu; (6) Déjà-vu; (7) "I feel as if I have dreamed the things that are happening"; (8) "Feeling of repetition of facts, activities or words"; (9) "Feeling that I already knew the people and places."

The area most frequently involved in the beginning of ictal automatisms is the periamygdaline region (uncus, amygdaline nuclei, deep temporo-insular cortex in the anterior part of the Sylvian fissure) (Fenton, 1981; Jasper, 1958). However, Jasper (1964) showed that stimulation of these structures only produces automatic behavior in 50% of the cases and that this behavior is not produced while the postdischarge is limited to the amygdala or the hippocampus; for this behavior to be produced, activity must extend to the medial diencephalon and the cerebral cortex and usually to the contralateral amygdala–hippocampal complex.

Over the past few years, great effort has been devoted to the analysis of the biochemical aspects of psychotic disorders on the one hand, and the pharmacological control of epilepsy on the other. Assuming that some epileptic phenomena (such as certain seizures of temporal origin and the interictal schizophreniform psychoses) can be considered as models in the study of primary schizophrenia, we must suppose the existence of biochemical changes which are in some way similar or complementary. Trimble (1982) emphasizes the existence of some type of relationship between psychosis and epilepsy through the intervention of dopamine: while dopamine antagonists eliminate the psychosis but lower the threshold for convulsions, the dopamine agonists raise the threshold for convulsions but provoke or aggravate the psychosis. Maynert et al. (1975) show that any treatment that increases the monoaminergic transmission modifies the levels of convulsions; drugs which increase the central monoamine levels, such as the tricyclic antidepressants, can provoke convulsions.

The pharmacological handling of primary schizophrenia and of schizophreniform psychosis is similar, underlining the existence of common neurophysiological mechanisms: both the one and the other respond systematically to groups of drugs which produce a block of the dopaminergic receptors (Toone, 1981). The majority of the psychotropic drugs, such as antipsychotic drugs, are epileptogenic. Crow et al. (1977) suggest that neuroleptic drugs exert their therapeutic actions in schizophenia and, in particular, on positive symptoms such as delusions, hallucinations, and thought disorders, blocking the dopamine receptors in the accumbens nucleus. The pattern of convulsion activity would go from the hippocampus and the amygdala to the septal region (Heath, 1976); the existence of important connections between the amygdaline nuclei and the septal nuclei and the mesolimbic dopaminergic system would constitute an ideal substratum for the development of psychiatric changes in patients with epilepsy of the temporal lobe. One of the principal pathways of the limbic system is the fornix which transmits information from the hippocampus to the accumbens nucleus and the septal area and vice versa. In turn, the stria terminalis interconnects the amygdala with the septal area.

It has also been suggested that the accumbens nucleus serves as an interphase between the limbic and motor systems, and that the convulsive activity of the amygdala and the hippocampus does not extend to the motor system unless the accumbens nucleus also participates (Aird, Masland & Woodbury, 1984). This would convert the accumbens nucleus into the central point in both the diffusion of the convulsive activity and in the action of neuroleptic drugs on schizophrenia.

The kindling effect is particularly easy to produce in the limbic system, especially in the amygdala. It is particularly interesting to note the fact that the kindling of the dopaminergic systems does not lead to convulsions but rather to changes in behavior and these changes can be inhibited with drugs which are antagonists of the dopamine receptors. Since the dopamine antagonists raise the threshold for convulsions, the diffusion of convulsions can be inhibited in response to kindling

stimulation, but subictal activity can be increased, producing changes in behavior and chronic alterations in the neuronal function of the limbic system which are responsible for personality disorders and psychiatric changes (Trimble, 1981).

In animals, subconvulsive limbic stimulation can produce behavioral changes, correlative to changes in the activity of the neurotransmitters (Adamec, Stark-Adamec, 1983; Stevens & Livermore, 1978). In human subjects, the maintained subictal activity would be responsible for the personality changes observed in patients with epilepsy of the temporal lobe (Beard & Fedio, 1977; Geschwind, 1983) and, in the long term, for the temporary presence of psychotic episodes. Heath and Mickle (1960) have shown, on the other hand, that during psychotic episodes polyspike and spike-wave discharges in the amygdala, the hippocampus and the septal area appear that are not always recordable with surface electrodes but that can be recorded with chronically implanted subcortical electrodes.

Since schizophrenia at least seems to be an illness linked to a certain age range (adolescence), it would be necessary to assume the existence of some genetico-maturational defect which only becomes evident during the later maturation of the nervous system. Fish (1975, 1977) proposes the concept of pandismaturation found in children at high risk of schizophrenia and which implies a generalized neurointegrative disorder. Marcus et al. (1981, 1985) found the presence of mild neurological signs that include perceptual deficits, defects in motor coordination, in left–right orientation, in balance, in motor control, etc., in these children. Mirsky and Duncan (1986) propose the existence of schizophrenogenic abnormalities as the biological factor underlying schizophrenia which would lead, during adolescence, to the appearance of a neurointegrative deficit. This deficit would become apparent in cognitive, perceptual affective disorders, etc.

To sum up, a progresively larger quantity of information related to the possible neurophysiological mechanisms underlying psychiatric disorders and, particularly, schizophrenia has been accumulated over several decades. The similarity found between certain types of schizophrenia and the disorders which can accompany epilepsy of the temporal lobe, whether they be interictal psychoses (short psychoses after several years during which the patient has presented complex partial seizures) or ictal psychoses, has been of special interest. Everything indicates that mental-subjective phenomena are unleashed with the activation of the amygdala–hippocampal complex either through the use of direct electrical stimulation (Halgren et al., 1978; Gloor et al., 1982) or in the case of epileptic seizures. The existence of the intervention of the limbic dopaminergic system and of a reciprocal action on the antipsychotic and anticonvulsivant drugs would seem to be sufficiently well established. It would be necessary to assume the existence of some genetico-maturational defect in this system in the case of primary schizophrenia as some authors have suggested.

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