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Summary

Surgical treatment of hemispheric epilepsy has progressively evolved from anatomical hemispherectomy to functional hemispherectomy and more recently to hemispherotomy. These developments in the surgical technique have to a large extent avoided the complications associated with large brain excisions and at the same time maintained the excellent seizure outcome associated with the surgical treatment of hemispheric epilepsy. We review the evolution of the surgical procedures, indications for surgery and the surgical outcomes of hemispherotomy series published in literature to date.

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Introduction

Hemispheric epileptic disorders often produce catastrophic epileptic syndromes in children that manifest or progress to marked unilateral neurological deficits, pharmaco-resistant epilepsy, and very frequently (if not always) result in cognitive dysfunction in the absence of adequate surgical treatment. These syndromes if not recognized in time, result in a dismal picture of a spastic hemiplegic child with intractable epilepsy and mental retardation. The persistence of these problems into adulthood paints an even more dismal picture because the outcome after surgery will only be good with respect to seizures whereas the cognitive dysfunction is there to stay with no hope for improvement. On the positive side, these syndromes when identified and treated surgically without delay, probably offer the best outcomes among all surgical procedures for epilepsy.

Milestones in the Evolution of Hemispherectomy

1928

Anatomical Hemispherectomy (AH) was first introduced for the treatment of diffuse infiltrating gliomas by Walter Dandy between 1923 and 1928 [1].The main contribution of this work on five patients with non-dominant gliomas was that this surgery was technically feasible and patients could not only retain consciousness but also recover some motor function. However, the patients died from either postoperative complications or disease progression.

1938

Anatomical Hemispherectomy for Seizures
McKenzie from Toronto, reported the first case of hemispherectomy for seizures in a 16-year-old patient who was cured of seizures following the surgery [2].

1950

The First Major Series (12 patients) of hemispherectomy for seizures was reported by Krynauw [3]. This surgery with excellent results gained widespread popularity in the first decade and by 1961, there were reports of over 260 cases worldwide for surgical treatment of infantile hemiplegia.

1966

Superficial Cerebral Hemosiderosis (SCH)
Oppenheimer and Griffith reported long-term complications following anatomical hemispherectomy [4]. This syndrome, which was later referred to as „Superficial Cerebral Hemosiderosis" manifested as neurological worsening, hydrocephalus and proceeded to mortality [5]. Autopsy findings demonstrated the presence of iron deposits on the residual brain, with granular ependymitis and were characterized by the presence of a membrane lying on the ventricular wall and hemispherectomy cavity. The fluid in the cavity was brownish and contained iron pigments. This complication occurred after a mean interval of 8 years in about 25% of cases and had a mortality of 30-40%. The increasing awareness of this problem led to the abandonment of this surgery. Decreasing the amount of brain removal led to lowered incidence of complication, but also reduced the seizure outcome.

1968

Hemidecortication
The search for alternative surgical strategies for the surgical treatment of hemispheric epilepsy without the long-term complications of anatomical hemispherectomy began in the late sixties. Ignelzi and Bucy reported the procedure of hemidecortication as an alternative to anatomical hemispherectomy [6].

1970

Modified Anatomical Hemispherectomy
Modifications to the technique of anatomical hemispherectomy (AH) began with the description of modified AH by Wilson [7], which was later popularised by Adams [8]. Following AH, the foramen of Monroe is plugged with muscle and the convexity duramater is stripped off the cranial vault and attached to the tentorium

and the falx, thus decreasing the subdual space but increasing the extradural space. Alternative techniques were described later by Dunn (duroplasty) [9], Matheson (omental vascularized flaps) [10] and Sorano (silicon prosthesis to fill the cavity) [11].

1974

Functional Hemispherectomy

Many groups to avoid the problem of SCH did subtotal hemispherectomy. But the procedure being subtotal, though avoiding the complications, gave seizure results, which were suboptimal. This phase of hemispherectomy surgery however led onto the realisation that parts of the hemisphere could be left in situ but could be disconnected. This therefore led to a major landmark in the history of hemispherectomy surgery with the introduction of the procedure of functional hemispherectomy by Rasmussen and Villemure [12, 13]. This procedure was noted to have comparable seizure results with anatomical hemispherectomy and greatly reduced long-term complications of AH.

1992

Hemispherotomy

The evolution of functional techniques in hemispherectomy led to the description of hemispherotomy, which can be viewed a radical hemispheric tractotomy. Villemure first reported the lateral hemispherotomy approach centered on the insula called Peri Insular Hemispherotomy (PIH) in 1992 [14, 15]. In this approach, the ratio of disconnection to resection was maximal. A vertical hemispherotomy approach was also described the same year by Delalande [16, 17]. Modifications of the lateral hemispherotomy approach were also subsequently described [18 - 20]. All these approaches are based on the concept of maximal disconnection and minimal excision. In the past decade, the technique of hemispherotomy (irrespective of actual variant used) has become standard of surgical care for hemispheric epilepsy.

Indications for Surgical Treatment of Hemispheric Epilepsy

Indications for hemispherectomy parallel those for the surgery for epilepsy in general with a few unique considerations. Because this is primarily a disease of childhood, the plasticity of the brain and the noxious effects of frequent uncontrolled seizures and antiepileptic medications (at high doses) on the developing brain needs to be considered. Added to this would be the social implications of a debilitating disease and the lost time at schooling due to the disease. These considerations need to be factored in while the decision to intervene is taken. On the other hand, the morbidity of a major surgery at a young age and the possibility of increased neurological deficits in some cases needs to be well appreciated and weighed against the substantial gains offered by surgery towards seizure relief and long-term functional outcome.

Any patient being considered for hemispherectomy needs to fulfil certain criteria:

1 Medical intractability is an absolute requirement though for hemispheric epilepsy, long exhaustive trials of anti convulsants may not be necessary as most often the seizure frequency is very high. Also some etiologies like Rasmussen's encephalitis, Sturge Weber syndrome and cortical dysplasia almost always have intractable epilepsy.
2 Contralateral hemiplegia should be present. If hemispherectomy is done prior to maximal hemiplegia, digital dexterity and foot tapping may be lost but the patient will be able to walk and use proximal muscles of the upper limb. Sometimes this loss of function may have to be accepted as the cost of control of debilitating seizures and cognitive decline. In other cases, hemispherectomy may be done when the distal power of upper and lower limbs become completely lost.
3 Neurodevelopmental retardation is usually present due to the interference of frequent seizures on the developing normal hemisphere. This would therefore be a relative prerequisite for hemispherectomy. A thorough neuropsychological evaluation to establish base line data and to document integrity of the "good" hemisphere is essential prior to surgery.
4 The hemisphere contralateral to the hemiplegia should be demonstrated by radiological (MRI/CT) and functional (scalp EEG, EEG video telemetry, PET, SPECT) imaging to have a diffuse abnormality. More importantly the remaining hemisphere should be normal to have a good result following seizures. Spread of epileptiform discharges to the normal hemisphere on EEG or even rare independent discharges on the normal side however does not imply a poor response to surgery.

Surgically Remediable Hemispheric Epileptic Syndromes

Infantile Hemiplegia Seizure Syndrome (IHSS)

IHSS is a descriptive term that refers to unilateral paralysis noticed in early childhood as a result of various pathologies affecting one hemisphere in utero or perinatally. Two thirds of the patients affected will develop seizures at some time during childhood, which may be refractory to antiepileptic medication. Often the epilepsy is of a catastrophic nature and, if not treated early can be a major factor that leads to progressive developmental retardation. Many different etiologies including migrational disorders are often grouped together under this term IHSS. However with the advent of modern imaging techniques, we favour the view that

the term IHSS should be restricted to only unilateral hemispheric insults occurring during gestation or at birth. Imaging reveals hemispheric atrophy with dilated ventricular system. There may be evidence of middle cerebral artery infarction and/or associated porencephalic and subarachnoid cysts.

Rasmussen's Encephalitis

This is a chronic childhood encephalitis manifesting with intractable epilepsy and progresses almost always to hemiplegia and cognitive dysfunction. 50% of patients have a preceding viral illness, though a clear viral etiology has not been documented. An autoimmune basis has also been suggested. These patients typically present with focal motor seizures though other forms are also known and half of the patients progress to epilepsia partialis continua. Though this illness is typically unilateral, there have been sporadic reports of bilateral disease. Radiological and functional imaging reveals the slowly progressive unilateral destructive nature of the disease.

Sturge Weber Syndrome (SWS)

Patients with SWS (encephalotrigeminal angiomatosis) usually present with progressive hemiparesis, seizures and mental retardation. Radiological studies show the pial angiomatosis and intracranial calcifications. Both localised and diffuse forms of the disease are known but they are almost always unilateral. Patients with focal disease may have normal intelligence and may be candidates for localised resections. On the other hand diffuse SWS often progresses rapidly to marked developmental retardation, which is related to damage to the hemisphere of venous origin.

Disorders of Neuronal Migration

Hemimegalencephaly is a hypertrophic neuronal migrational disorder that presents with an early onset of seizures, mental retardation, hemiparesis and frequently hemianopia. It can present with a large head and may be associated with linear nevus sebaceus or chronic linear nevi. Radiological imaging shows a markedly enlarged hemisphere with a thickened cortical mantle. On pathological examination, pachygyria is seen and typical microscopic features include loss of cortical architecture, giant neurons, neuronal heterotopia and gliosis. On the other hand, diffuse hemispheric nonhypertrophic cortical dysplasia occurs less frequently and manifests with a smaller hemisphere with a variety of migrational abnormalities.

Other Hemispheric Syndromes

A variety of acquired pathologies can affect predominantly one hemisphere. These include cerebrovascular accidents due to thromboembolic phenomena due to heart disease or children undergoing heart surgery or extracorporeal membranous oxygenation. In developing countries, post meningoencephalitic sequela form a not uncommon cause for hemispheric epilepsy. Cerebral infarction secondary to severe dehydration and severe hypotension can also present likewise. Cranial traumas, brain damage secondary to massive intracranial Arterio-Venous Malformation (AVM) bleeds are more infrequent causes. Very rarely, West's syndrome and Lennox-Gastaut syndrome may have predominantly unilateral abnormalities but would need to be very carefully selected before contemplating hemispherectomy.

When to operate?

Frequent seizures have a deleterious effect on the normal maturation of the brain by secondary pathological changes in the brain. Axonal growth, migration and synaptogenesis depend on normal electrical fields, appropriate environmental stimuli and physiological stability. In addition, transient repetitive anoxia induced by prolonged and frequent seizure activity produces cumulative brain damage. Post ictal depression and inter ictal spiking also may result in depressed neuronal maturation and damage. Synaptogenesis has also been shown to be greatly affected by continuous sensory deprivation during critical periods of brain development, which is the case in high frequency seizure disorders. Damage to limbic cortices by frequent interictal discharges may explain progressive psychosocial decline often seen in these disorders. High doses of antiepileptic medications frequently given as combination chemotherapy also have deleterious effect on the developing brain. Added to this is the effect of disturbed social integration and lost schooling due to frequent seizures on brain development. On the other hand, neurological worsening after hemispherectomy also needs to be considered. In general, hemispheric insults sustained in utero or in childhood stimulate the development of brain functions in the healthy hemisphere. There has also been evidence to support that in cases where the disease started later in childhood, early surgery helps the shift of functions especially language to the contralateral side. But the exact age at which the normal plasticity of the brain ceases to transfer brain functions has not yet been defined.

All these considerations make a case for early surgery in cases of catastrophic childhood epilepsy especially in certain syndromes, which are known to progress to intractable epilepsy and developmental retardation like Rasmussen's syndrome, major congenital malformations and Sturge Weber syndrome. In some cases, if the deficits are not maximal, there may be a case to wait till they

do become maximal. However when clinical data suggest that this would become maximal eventually and progressive cognitive decline is documented to occur, early surgery may be offered at the expense of postoperative neurological worsening. In the pediatric population, the language and distal motor power return and the child will be able to walk and run with solely the loss of digital dexterity remaining.

Surgical Approaches

Anatomical Hemispherectomy

The classical AH involved resection of the entire hemisphere sparing the basal ganglia after ligation of the major vessels. But this procedure has virtually been abandoned due to the long-term complications associated with it.

Hemidecortication

This involves a large removal of the grey matter with preservation of the white matter and avoids a large opening of the ventricle. However completeness of removal of the entire cortex in this procedure is difficult to determine and the incidence of hydrocephalus is higher compared to other present day techniques.

Functional Hemispherectomy

This surgery was based on the concept of partial anatomical resection and complete physiological disconnection of the residual unresected brain. The long-term complications of AH were avoided to a large extent with this procedure and provided comparable seizure results.

Hemispherotomy

Hemispherotomy approaches represent the latest stages of evolution of functional hemispherectomy. It can be best viewed as a „radical hemispheric tractotomy". The ratio of disconnection to resection is maximal with this approach. There are two main hemispherotomy approaches with a few variants:

1 **Lateral Approach** is centered on the insula and most ipsilateral connections are disrupted when the approach is taken to the ventricle. Following this a parasagittal callosotomy is done to disconnect interhemispheric connections. Four variants of the main central theme of lateral hemispherotomy approach have been described:

   a. Peri insular hemispherotomy
   b. Hemispheric deafferentation
   c. Trans sylvian keyhole functional hemispherectomy
   d. Trans opercular hemispherotomy

2 **Vertical Hemispherotomy**
   This approach described by Delalande is through a parietal parasagittal approach to the ventricle by the creation of a cortical shaft in the central region. The other disconnections are performed within the ventricle.

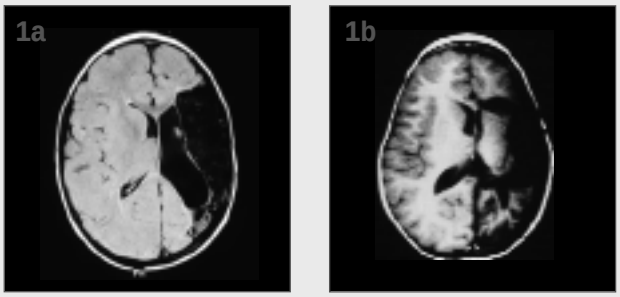

Figure 1a: T1 weighted axial MRI scan of a 7 year old boy presenting with infantile hemiplegia seizure syndrome showing a large atrophy of the left hemisphere largely in the territory of the middle cerebral artery with dilatation of the ipsilateral lateral ventricle.
Figure 1b: Postoperative T1 weighted axial MRI scan showing the peri insular window and the disconnections made.

Peri Insular Hemispherotomy

The scalp incision and craniotomy required to perform the entire disconnection of the hemisphere is quite small and is centered on the insula. It need only be big enough to give adequate exposure of the insula and circular cistern surrounding this. The rest of the disconnection can be comfortably done from within this exposure and is easier if the ventricular system is large due to the destructive disease of the hemisphere. Electrocorticography and continuous contra lateral EEG monitoring may be done for research purposes but will not change the surgical strategy. The surgery has several distinct stages.

Supra Insular Window

The supra insular window is created by incising the pia mater 5-8 mm above the sylvian fissure. As many of the vessels traversing the window need to be preserved. The opercular cortices are then removed sub pially either by aspiration or en bloc. This gives exposure to the circular cistern. From there, the incision is carried towards the ventricle which is then completely opened from anterior to posterior. This would therefore disrupt all corona radiata fibers proceeding from the frontal

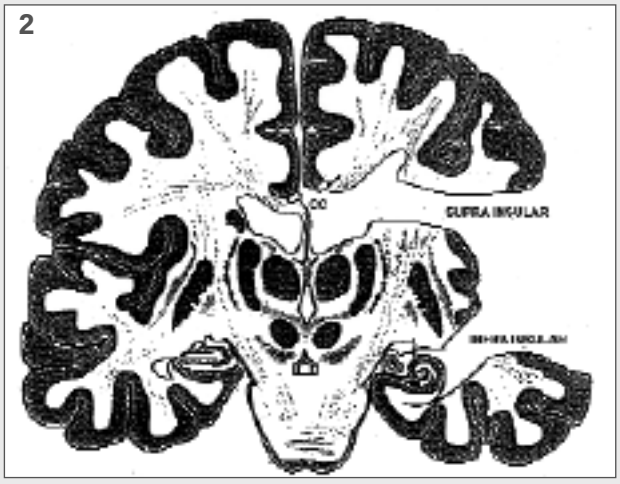

Figure 2: Diagrammatical representation of peri insular hemispherotomy in the coronal plane demonstrating the supra and infra insular windows and the site of the parasagittal callosotomy.

and parietal lobes at the level of the corona radiata internal capsule transition.

Infra Insular Window

The infra insular window is also made in a similar fashion below the sylvian fissure. The opercular cortex is removed and the ventricle is entered and opened widely and then connected across the trigone to the supra insular window. The intraventriclar structures are inspected and large cottonoids are placed in the ventricle to avoid blood spillage into the ventricle.

Corpus Callosotomy

From the supra insular window, the location of the corpus callosum is identified with reference to the septum pellucidum and the roof of the ventricle. A para sagittal callosotomy is performed from within the ventricle. The identification of the peri callosal arteries and following these anteriorly and posteriorly facilitates the callosotomy. The whole genu and the splenium need to be sectioned to interrupt all interhemispheric connections.

Frontobasal Disconnection

The mesio basal frontal cortex still has residual connection through the anterior commissure and this is disconnected through an incision starting from the anterior end of the callosal incision proceeding parallel to the sphenoid ridge and going up to the basal pia through the entire thickness of the anterior end of the suprainsular window.

Radical Amygdalectomy and Anterior Hippocampectomy

In the antero medial part of the temporal horn, the amygdala is removed and its removal can be more radical compared to standard temporal lobectomy. The anterior part of the hippocampus upto the level of the choroid fissure is then removed. These form the only parts of the brain that needs to be resected in the surgery. The amygdala does not have well defined anatomic borders and an injudicious estimation of the amygdala can result in an entry into the basal ganglia. If the line of resection of the amygdala were kept at the level of the roof of the temporal horn, this would avoid injury to the deep ganglionic structures.

Posterior Hippocampotomy

The main output of the temporal lobe is through the hippocampus and fornix. This is disconnected by the posterior hippocampotomy, which is essentially the division of the fornix. This location for the fornix division can be reached when the medial ventricular wall is incised starting from the posterior end of the splenial disconnection and continued towards the fissure and this would interrupt the fornix.

Insula

The insula though disconnected predominantly still has anatomical continuity with the basal ganglia. The insular cortex can be resected between the middle cerebral artery vessels or alternatively it can be disconnected at the level of the extreme capsule or claustum.

Results

Our series of 79 functional hemispherectomy procedures includes 47 cases of peri insular hemispherotomy. We retrospectively analysed the clinical profile and results of surgical treatment of these patients who underwent PIH. There were 27 males and 20 females in this series. The mean age of this group was 12 years (1- 44 years). 27 cases were left sided and 20 were on the right side. There were 26 cases of congenital pathologies, which included 19 cases of infantile hemiplegia seizure syndrome; three cases of hemimegalencephaly and 4 cases of non-hypertrophic diffuse migrational disorders. 20 cases had acquired etiologies which included 13 cases of Rasmussen's encephalitis, 2 cases of cranial trauma, 2 cases of sequelae following meningoencephalitis, 2 cases of cerebrovascular accidents and 1 case with anoxic brain injury. One case had an undetermined etiology with the only factor identified being neurofibromatosis. The average duration of the seizure disor-

der was 8.3 years (9 months to 43 years). 4 patients had history of previous surgery for epilepsy.

In this series we had 2 postoperative deaths (4%). One patient, who was one of the earlier cases, had massive brain swelling on the 3rd postoperative day from which he did not recover. We attributed the brain swelling to the continuous peri insular window, which necessitated the ligation of many peri insular vessels. Since then, we have modified our strategy to operate between vessels through multiple windows. The other patient had a sudden death for which no reason was found. Of the remaining patients, we have sufficient follow up data for 38 patients and this information was used for the analysis. Engel's seizure outcome classification was used to classify surgical outcome. 34 patients (89%) were in Engel's Class I, 3 patients (8%) in Class II and 1 (3%) in Class IV. Therefore in this series, 37/38 (97%)of the patients were free/almost free of seizures (Engel's Class I and II) after a mean follow up period of 4.2 years (0.5-10 years). With seizure cessation, there was a marked improvement in functional status with a definite „catch up" in cognitive domains seen in the pediatric group. Anti epileptic medication could be gradually tapered and stopped in a large proportion of patients.

Discussion

There are 7 published case series of hemipsherotomy in literature to date **(Table 1)**. These include various techniques. Peri insular hemispherotomy [15,18,19] is a lateral hemispherotomy approach. The other variants of this approach include hemispheric deafferentation, trans opercular hemispherotomy and trans sylvian keyhole functional hemispherotomy [20-22]. The other approach described is the vertical hemispherotomy approach of Delalande [17]. We analysed the cumulative data of the published series of hemispherotomy and our present series to date. There were a total of 183 patients (also includes 5 cases of hemidecortication which were described together with PIH in the series of Kestle et al). Of the 161 patients for whom follow up data were available, there were 132 in Engel's Class I (82%) and another 18 patients (11%) in Class II. The mortality or grave morbidity in all these series totally account for 5 cases (2.7%). Hydrocephalus necessitating treatment was seen in 18 patients (10%). Cases with hemimegalencephaly formed the majority of patients with hydrocephalus. This could be due to the higher amount of debris in the ventricle because of a much larger amount of brain tissue handled in this procedure compared to atrophic hemispheres. The incidence of hydrocephalus was higher with the vertical approach (10/51 cases; 20%) and transopercular approach (5/34 cases; 15%) when compared to our series of peri insular hemispherotomy (2/47; 4%). Nevertheless the whole cumulative series has only 10% hydrocephalus, which compares favourably with earlier reports of anatomical hemispherectomy and hemidecortication [23,24]. More significantly long-term complications like SCH have not yet been reported in series of hemispherotomy though quite long follow up periods of up to 10 years are available for study. But it would still be too early to state definitely that this would not occur as data from anatomical hemispherectomy show that SCH are known to occur after more delayed periods [5].

Conclusion

Patients with maximal or near maximal hemiplegia with intractable epilepsy with radiological and functional imaging demonstrating unilateral hemispheric abnormality should be considered as candidates for hemispherectomy. In the pediatric population, the „window of opportunity" that is offered should not be lost due to a delay in referral for surgical control of seizures. Hemispherotomy irrespective of the actual variant performed gives total or almost seizure free status in over 90% of cases with the mortality/serious morbidity rate below 3%. The main advantage of this procedure when compared to anatomical hemispherectomy includes shorter operative time, lesser blood loss and much better postoperative course. Despite very long follow up periods, there have been no reports to date of long-term complications akin to anatomical hemispherectomy.

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Table 1

	Series	N	Seizure Outcome	Class I	Follow up	Complications
1	**Villemure[15] 1995**	11	Seizure free 9/11 >95% reduction 2/11	82%	0.3-3 yrs	Hydrocephalus 1(9%)
2	**Schramm[20] 1995**	13	Seizure free 11/12 >75% reduction 1/12	92%	Mean 1 yr	Hydrocephalus 1(8%)
3	**Delalande[16] 2000**	53	Class I : 41/52 Class II: 10/52 Class IV:1/52	80%	1-8 yrs	Death 1(2%) Hydrocephalus10(20%)
4	**Shimizu[22] 2000**	34	Class I: 18/27 Class II: 2/27 Class III: 6/27 Class IV: 1/27	67%	> 1 yr	Grave morbidity 1 (3%) Hydrocephalus 5(15%)
5	**Kestle[19] 2000**	16 +	Class I: 14/16 Class II: 2/16	88%	Median 3 yrs	Nil
6	**Schramm[21] 2001**	20	Class I: 14/16 Class III: 1/16 Class IV: 1/16	88%	Mean 3.8 yrs	Death 1 (5%) Infection 1 Temporal cyst 1
7	**Daniel[18] 2001**	6	Class I: 6/6	100%	Mean 1.1 yrs	Nil
8	**Villemure 2003** **(Unpublished)**	47	Class I: 34/38 Class II: 3/38 Class IV: 1/38	89%	4.2 yrs (0.5-10 yrs)	Death 2 (4%) Hydrocephalus 2(4%) Remote bleed 1

Case series of hemispherotomy series to date with seizure outcome and complications. The techniques employed are peri insular hemipsherotomy, hemispheric deafferentation, trans opercular hemispherotomy, trans sylvian keyhole functional hemispherotomy and vertical hemispherotomy. In study 5 by Kestle, 5 cases of hemidecortication are also included.
The seizure outcome in most studies is classified based on Engel's seizure outcome classification (Class I to IV).
Note that patients in Study 1 and 7 are also included in the analysis of results of present study 8 (Villemure 2003).

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