Recent knowledge concerning the neural development disorder hypothesis of schizophrenia with interpretations and observations of the Wagner brain case.

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1. Introduction

We became interested in the relationship of the scientific observations of nervous disorders of the brain and delusions, with the opportunity to learn of the subject which has become evident in recent years through the cerebral observations upon vice principal Wagner, which was the first and most famous paranoia case in Germany at the beginning of the twentieth century. We have examined the bibliography and abridged translations of reports on this subject in combination with results cited in a recent thesis concerned with research into schizophrenia.

2. Summary of the Wagner case [1]

In 1913 the 38 year old vice principal Wagner murdered his wife, four children - five people in all - with a cudgel and knife, in his own home. He then went directly to visit the village of Muehlhausen in connection with his teaching, and carried out arson in four places and shot a number of people one after another. Eight people died instantly and twelve people were seriously injured. Wagner was caught there, and was taken to Tubingen University hospital to observe his mental condition. He received six weeks expert mental appraisal from Dr Gaupp, following which he was isolated in a private room for the 24 years up to his death in 1938, at the mental hospital.

What happened after this and a summary of the report by Gaupp as described below.

Wagner's family history: Mother's 2 siblings were schizophrenic, a great uncle harboured religious delusion of grandeur. The father died of alcohol dependence, and the family were burdened with the father's debts due to drinking. The mother was

susceptible to pessimistic melancholy, she was prone to harbour unspecified idea of persecution and was a woman who had abnormal sexual desires.

Wagner's developmental history: he was afflicted by terrible dreams of persecution and fear from childhood, and showed anxiety of sensitiver and delusional psychopathy. When he was 18 years old, having become distressed by being liable for crime and addicted to masturbation, such that when thinking about the conversations with people around him, peoples words and gestures became distorted.

Inducement to the event: When he was 26 years old, after the bestiality, he was under the impression that there were rumours in the village about him, and that he was being stalked and persecuted, and delusion of persecution developed. Because of fears over whether he would be caught, he habitually carried two guns. It is said that he planned the massacre in Mühlhausen as retaliation, presumably for his perceived persecution.

Murder plan: the plan was honed over many years and was that "he would commit suicide by fire after committing arson in the Ludwinsburg district, deciding to kill all his siblings family, setting fire to the village after murdering all the adults in Muhlhausen". The killing of his family was thought to have been in order that they would not be shamed.

After entering the mental hospital: For a short while the violence of delusion was maintained, without any sense of guilt or regret. Later in the quiet environment (presumably of the private room), although there was a temporary relaxation in the disorder, even just before his death "even if hundreds had died, that would be nothing compared with my suffering" he was chagrined over the hitch in the murder plan.

Gaupp's interpretation: Wagner's complex disorder development was due to many factors, such as gene-bearing factors, environment, and experience , it was recognised that clarity of thought, purpose and action were retained, but there was no schizophrenia (supporting Kraepelin's paranoia). The autopsy observations upon the brain after death "no morbid observations with the naked eye. Microscopic examination revealed no results".

Whereabouts of brain after death: Due to miliary pulmonary tuberculosis, after death the brain was sent to Berlin Brain Research Centre, but was returned due to a deformation when it was fixed, but it was not clear where it went to. Bogerts discovered this brain specimen by chance at Düsseldorf University Vogt Brain Research Centre(Institut für Neuroanotomie und C. und O. Vogt Institut für Hirnforschung), and generated the report(original text source: Mehrdimensionale Psychiatrie, Gustav Fischer Verlag, Stuttgart, pp 78 - 89, 1997)

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3.Bogerts report [2]

After death Wagner's brain was divided into the right and left hemispheres, the right hemisphere being left hard in paraffin (ie without being sectioned or sliced), and the left-hand hemisphere was sectioned in the coronary direction, and every 50^{th} slice was stained. It was decided to slice the cerebellum also but no staining was undertaken. Consequently, structurally scientific

examination of continuous sections was possible only with the left-hand hemisphere.

The recognition of what was clearly diseased was the entorhinal area in the left parahippocampus region convex rear section, ie an impaction depth 2mm and length 2cm was seen in the central limbic system structure. The impaction was covered by a soft membrane, with a perforating branch fibre was passing through it where it should not, hence the cell layer was observed to have an abnormal structure. From this fact, no brain disease or external injury had occurred since reaching adult age, so it is suspected that the cause of this abnormality is limited growth disorder in the parahippocampal gyrus. The pathalogical change in Wagner's brain was located in the perforating branch which is a very important part of the cortex information process, and damage to the functioning of this part will lead to dissociation of emotional feelings and recognition (being able to emotionally systemise past and present experiences without adapting them to the actual situation). The neurological mutation of the limbic system in the area of the temporal lobe in the brain thus formed, is in agreement with the observations pointed out by the field of biological schizophrenia research. Consequently, the occurence of delusions is not adequately explained by Gaupp's developmental psychology, and further information on the tendences of brain disease must be requested.

4.Trends in brain imaging research into schizophrenia and the neural growth disorder hypothesis.

Due to progress in brain imaging research, some excellent results have been provided by biological research into schizophrenia. We will try to give an overview of the knowledge of brain imaging research which is considered to have contributed also to the neuro-scientific research into Wagner's brain.

In the latter half of the 1970's although much research into the expansion of the brain ventricles in schizophrenia using CT has been reported, it was difficult to specify the essential parts of the brain which permit the changes in shape. From the latter half of the 1980's onward, abnormalities in shape have been proven due to MRI. The change in brain substance has been pointed out to be associated with the hippocampus, amygdala, and the temporal lobes, especially the expansion of the brain ventricles and atrophy of the brain substance along with negative symptoms[3].

Furthermore, the significance of supplementing the observations of the schizophrenic brain after death was evaluated by MRI research. ie, without recognising gliosis by neuro-pathalogical observations, because of cell structure abnormalities in the form of nerve cell hyperplasm propagation imperfections from the ectodermal layer, there is no post-natal change in the original cause of schizophrenia, based upon the hypothesis[4] which seeks disorders in the nerve development process from the prenatal period. Embryologically the cell migration to the cortex is complete by the end of the 5 months fetus period, because of the fact that the gliosis against invasion of the brain has occurred on or after the prenatal middle period, it is suggested that disorders in the nervous system will have occurred by the middle of pregnancy. As the cause of this invasion, in addition to the chief genetic cause, there are reports which point out a correlation with eg., influenza infection while inside the mother's uterus during this time, RhD incompatibility, serious nutritional disorders, drug poisoning etc[5].,

On the other hand, regarding the follow-up research to prove post-natal abnormal changes in shape in the brain, the shrinkage proportions of both lateral cerebral hemispheres, right hemisphere of cerebellum and the corpus callosum of and the expansion proportion of the brain ventricles are larger in comparison with those of other people[6], and it is suggested that the advanced pathalogical change caused the shape change even after the onset of schizophrenia.

Research which investigated the relationship with the blood flow metabolism in the brain was carried out in accordance with PET and SPECT etc., however the reality distortion (auditory hallucinations and delusions) symptoms exhibited positive correlation with the left lateral parahippocampal gyrus and the left corpus striatum blood flow, whereas a negative correlation was seen with the right posterior part of cingulate gyrus[7]. Regarding lack of mental exercise or dissociation (non-conforming emotions, thinking disorders, poverty of conversation content) symptoms, there was correlation with the blood flow of various parts, shown to be based upon various neural networks. Also, in separate research, the thinking disorders and tendency to exaggerate in patients who were never treated, exhibited a positive correlation with the blood flow in both sides of the frontal lobes and both sides of the temporal lobes, while the delusions, hallucinations and distrust were seen to exhibit a negative correlation with the blood flow in the cingulate gyrus, the left temple, the left parietal lobe, but after the positive symptoms were disappeared by treatment, the blood flow correlation was shown to be associated only with the negative symptoms[8]. This indicated that different neural networks contributed according to the type of the positive symptoms. On the other hand, the change in the glutamic acid pool in the schizophrenic patient during the chronic period has been proved to vary depending upon clinical type[9]. ie., in the proven case of emotional dullness the frontal lobe Brodmann 10 field activation fell, while in the case of proven delusions, the right parietal lobe Brodmann 40 field activation, or the left temporal lobe Brodmann 38 field activation fell respectively. Parts such as these which are the areas of the brain which manage knowledge and advanced judgement, are considered likely to be the cause of neural function disorders.

In research into neural communication functions, based upon changes in the brain after death, the hypothesis assuming an increase of the dopamine D2 receptor in the corpus striatum neucleus accumbens has attracted attention, but recent research using PET however, has been reported upon negatively many times[10]. The dopamine increase in the left amygdala, the decrease in the KA (kainic acid) in the left hippocampus, the decrease of the part which uptake GABA in the left hippocampus etc., and neither research suggesting the presence of neuro-scientific abnormality in this area of the schizophrenia in some published literatures.

5.Conclusions

Thus far what has been shown by the many research suggests a correlation between the inner parts of the temporal lobe, the parahippocampal gyrus including especially the hippocampus, the subiculum gyrus, the inner olfactory cortex, and the schizophrenic positive symptoms. The inner olfactory cortex seen in the pathalogical change in Wagner's brain agrees with the Brodmann 28 field, located in the parahippocampus region gyrus. At this point information from the fields associated with the frontal lobe and the temporal lobe

etc, corpus striatum, amygdaloid body, thallamus, and hypothallamus, is collected by one of the cortex information process convergence centres. Although this part receives strong control of the dopamine nerves, this is influenced by the glutanic acid function. There are also reports of a fall in dopamine control in the inner olfactory cortex in schizophrenic brains after death.

Regarding the abnormal shape of the brain after death, although there have been many reports on research using MRI, these have not necessarily shown results which are in agreement.Negative reports have also been seen concerning the lateral ventricle expansion and brain volume.

There are various clinical types within schizophrenics, such as delusion types and dissociation types, because the possibility of changes due to clinical progress needs to be considered, in the future, comparative research considering things of this nature is thought to be necessary.

Research into in vivo by recent imaging analysis, with knowledge accumulated based upon postmortal brain research after death, has been examined comprehensively, but we would like the causes of schizophrenia and the starting mechanisms of various symptoms to be proven, starting with a clearer elucidation of the inner olfactory cortex as a first step, correlation of hippocampus and limbic system etc., with mental functions.

Theses related to research into brain imaging in schizophrenics, in addition, show recent knowledge of relationships between negative symptoms and hypoftrontarity, cell membrane creation and analysis by MRS, and correlations between differences in right and left hemisphere abnormalities (loss of left hemisphere dominance in the temporal plane) and serotonin influenced information transmission system etc., but we would like to omit these here, because they depart substantially from the interpretation of Wagner's paranoia development.

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