What is Anosognosia?
(updated March 2014)

Anosognosia is an awkward term introduced by neurologists a century ago “to denote a complete or partial lack of awareness of different neurological…and/or cognitive dysfunctions.” This definition comes from G.P. Prigatano, ed. The Study of Anosognosia, Oxford University Press, 2010, p.17. Anosognosia thus means lack of awareness or lack of insight. It is not the same as denial of illness; anosognosia is caused by physical damage to the brain and is thus anatomical in origin whereas denial is psychological in origin.

Anosognosia is very difficult to imagine or understand. Oliver Sacks, in The Man Who Mistook His Wife for a Hat (p.5), explained anosognosia as follows:

> It is not only difficult, it is impossible for patients with certain right-hemisphere syndromes to know their own problems – a peculiar and specific ‘anosognosia,’ as Babinski called it. And it is singularly difficult, for even the most sensitive observer, to picture the inner state, the ‘situation’ of such patients, for this is almost unimaginably remote from anything he himself has ever known.

Among neurological patients, anosognosia is seen most commonly in Alzheimer’s disease, Huntington’s disease, and traumatic brain injury and occasionally in patients with stroke (especially those involving the right parietal lobe) and Parkinson’s disease. Most patients with Alzheimer’s disease, for example, are aware that something is wrong early in the course of their illness but then lose all awareness of their illness as it progresses.

Anosognosia is also very important in psychiatry since approximately 50 percent of individuals with schizophrenia and 40 percent of individuals with bipolar disorder have anosognosia. It is the most common reason why individuals with schizophrenia refuse to take medication; since they do not believe that there is anything wrong with them, why should they? Impaired awareness of illness is not a new idea for psychiatric patients; in 1604 playwright Thomas Dekker has a character in The Honest Whore say: “That proves you mad because you know it not.” Research on anosognosia in psychiatry in recent years has been led by Drs. Xavier Amador and Tony David; their 2004 book, Insight and Psychosis: Awareness of Illness in Schizophrenia and Related Disorders, is an excellent summary of the early research.
Awareness of illness sometimes improves with treatment with antipsychotic medication, especially clozapine. Also very helpful is Dr. Amador’s book: *I Am Not Sick: I Don’t Need Help!*

It is now clear that anosognosia in psychiatric patients, just as anosognosia in neurological patients, is caused by brain damage associated with the disease. Since 1992, there have been 22 studies comparing the brains of individuals with schizophrenia with and without anosognosia. In all except two studies, there were found to be significant differences between the two in one or more anatomical structures. Since anosognosia involves a broad brain network concerned with self-awareness, a variety of anatomical structures are involved, especially the anterior insula, anterior cingulate cortex, medial frontal cortex, and inferior parietal cortex. Three of the positive studies included individuals with schizophrenia who had never been treated with medications so the observed brain changes cannot be attributed to the treatment.

The following is a **summary of the studies of anosognosia in the brains of individuals with schizophrenia**, beginning with the most recently published.

- **Awareness of illness is associated with changes in the brain which can be seen microscopically.**

At the Mental Health Research Center in Moscow, sections of the brain from 24 deceased individuals with schizophrenia were examined microscopically. The brain areas chosen were two parts (supramarginal and angular gyri; BA 40 and 39) of the inferior parietal lobule, known to be important in anosognosia. The 24 individuals were assessed for awareness of their illness postmortem by examining their medical records; explicit denial of illness, refusal to take medication, and failure to follow their treatment plan were used as indicators for poor awareness of illness. Among the 24, 9 had good awareness and 15 had fair or poor awareness of illness.

The results of the study showed a 21 percent reduction in glial cells (specifically obligodendroglia) in the brains of the individuals with anosognosia (fair or poor insight). Those with anosognosia differed statistically from the normal control brains (p=0.04) and at the borderline statistically from those without anosognosia (p=0.055). The brains of the individuals without anosognosia (good insight) did not different from the normal controls. This is the first study which assessed microscopically the brains of people who have died with schizophrenia, some of whom had anosognosia and some of whom did not. Those with anosognosia had fewer glial (obligodendroglial) cells.


- **Awareness of illness is associated with hemispheric asymmetry in schizophrenia.**

In Canada at the University of Toronto, 52 individuals with schizophrenia were assessed for awareness of illness (using the relevant item on the PANSS) and underwent MRI. Lack of awareness of illness was strongly correlated with both severity of illness (p<0.01) and with total white matter volume (p<0.01). Hemispheric asymmetry was evident with the right hemisphere having less volume than the left hemisphere in patients with impaired awareness of illness,
specifically in the anterior end of the inferior temporal lobe (p=0.05); the dorsal lateral prefrontal cortex (p=0.003); and the inferior parietal lobe (angular gyrus) (p=0.05). These findings are consistent with the occurrence of anosognosia in some individuals with strokes when the stroke occurs in the right hemisphere. It suggests that awareness of illness in schizophrenia is probably caused by damage more to the right hemisphere. Individuals with schizophrenia who retain their awareness of illness probably have less damage to these specific right hemisphere areas.

The authors of the study also noted that persons with schizophrenia vary in their degree of anosognosia: "They can have equally bizarre delusions or perceptual disturbances but can be quite dissimilar in their ability to recognize that these experiences arise from their mind rather than a part of objective reality." This is one of the most puzzling aspects of schizophrenia for family members.


- **Awareness of illness is associated with the function of the medial prefrontal cortex, insula, and inferior parietal lobule.**

In the Netherlands, 47 individuals with schizophrenia and 21 normal controls were assessed by functional MRI. They were asked to do tasks which required them to think about themselves (self-reflection) while having their brains scanned. Individuals with anosognosia (less ability to think about themselves) showed significantly poorer activation in several brain areas, including parts of the frontal and parietal lobes. These were statistical group differences but they cannot yet be used to predict anosognosia in any given individual.

The following pictures illustrate such differences. They compare two individuals with schizophrenia, one of whom has good insight (high self-reflection) and the other of whom has poor insight (low self-reflection). Figure 1 shows much better activation in the insula and the inferior parietal lobule (IPL) in the individual with good insight. Figure 2 shows much better activation in the medial prefrontal cortex (MPFC) in the individual with good insight.

Awareness of illness is associated with the function of midline brain structures.

In Finland, 21 patients with schizophrenia and 17 normal controls underwent both structural magnetic resonance imaging (MRI) and functional MRI, during which time they were asked to answer specific questions about insight, e.g., “If someone said I had a mental illness they would be right.” Insight was associated with activation of brain midline structure, specifically posterior cingulate, medial prefrontal cortex, and frontal pole, brain areas known to be associated with...
self-awareness. The authors acknowledged that “the present findings…cover only a portion of the neuronal circuitries involved in the processing of insight.”


- **Anosognosia is associated with impaired cerebral blood flow in the superior parietal area (precuneus).**

In France, 31 patients with paranoid schizophrenia and 18 normal controls were assessed for cerebral blood flow by single photon emission computed tomography. 21 patients had good awareness of their illness and 10 did not. Those with poor awareness of their illness showed poor cerebral blood flow to their precuneus bilaterally (p<0.001). There were no differences in the frontal lobes. The precuneus is part of the superior parietal lobe and known to be involved in self-consciousness, including awareness of one’s own emotional state.


These pictures show differences in blood flow to the superior parietal area (precuneus) in individuals with schizophrenia with impaired awareness of illness (anosognosia) (left) and preserved awareness of illness (right).

*Pictures courtesy of Dr. Eric Guedj and colleagues, Hospital de la Timone, Marseille, France.*

- **Anosognosia is associated with a decrease in gray matter.**

In Spain, 21 individuals with first-episode schizophrenia and who had never been treated were compared on MRI with 20 controls. Insight was assessed by using 3 items from the SUMD scale. Patients with poorer insight had a significant decrease in gray matter volume in medial superior frontal gyrus; inferior frontal gyrus; inferior temporal gyrus; and cerebellum.


- **Anosognosia is associated with widespread impairments in white matter.**
At New York University, 36 individuals with schizophrenia and schizoaffective disorder underwent diffusion tensor imaging (DTI), which assesses brain white matter integrity. Those with poorer awareness of their illness were significantly more likely to have impaired white matter function in the frontal lobe (e.g., left middle and right superior frontal gyri); temporal lobe (e.g., bilateral parahippocampal gyri); cingulate; thalamus; and basal ganglia (caudate and lentiform nucleus).

Antonius D, Prudent V, Rebani Y, D'Angelo D, Ardekani BA, Malaspina D, Hoptman MJ. White matter integrity and lack of insight in schizophrenia and schizoaffective disorder. *Schizophr Res.* 2011 May;128(1-3):76-82.

- **Anosognosia is associated with decreased cortical thickness.**

In Montreal 79 individuals with first-episode psychosis were assessed clinically and by magnetic resonance imaging (MRI). Poorer awareness of illness was significantly associated with having a thinner brain cortical layer in the left middle frontal gyrus, left inferior frontal gyrus, left inferior temporal gyrus, left and right precentral gyrus, and right occipital gyrus. Impaired awareness of need for treatment was significantly associated with a thinner brain cortical layer in the left middle and medial frontal gyri; parietal precuneus and supramarginal gyrus; temporal parahippocampus and superior, middle and inferior gyri; and middle occipital gyrus. The authors concluded that “insight involves a network of brain structures, and not only the frontal lobes as previously suggested.”


- **Anosognosia is associated with impairments in midline brain structures (posterior cingulate and precuneus).**

In England, 82 individuals with first episode psychosis and 91 normal controls were assessed on neuropsychological tests and by magnetic resonance imaging (MRI). 20 of the individuals with first episode psychosis “had no capacity to identify psychotic symptoms as pathological.” Compared with the other 62 individuals, those 20 had “significantly reduced global gray matter volume,” most marked in the left posterior cingulate cortex, the right precuneus, and the cuneus.


- **Anosognosia is associated with impairments of temporal and parietal areas.**

In England, 52 individuals with schizophrenia or schizoaffective disorder and 30 normal controls were assessed for awareness of symptoms and underwent magnetic resonance imaging (MRI). Those with poorer awareness of their symptoms had decreased gray matter volume in their left superior, left middle, and right inferior temporal gyri, as well as the right inferior parietal lobule and right supramarginal gyrus (all p<0.001).
• **Anosognosia is associated with decreased gray matter volume of the prefrontal cortex.**

In England, 28 outpatients with stable schizophrenia were assessed for insight and underwent magnetic resonance imaging (MRI). Lower levels of insight were moderately associated with decreased volume of the prefrontal gray matter, especially the inferior frontal gyrus.


• **No association between anosognosia and regional brain volumes.**

In Italy, 50 patients with schizophrenia and 30 normal controls were assessed for awareness of illness and by magnetic resonance imaging (MRI). No relationship was found between awareness of illness and the gray and white matter volumes in the frontal or temporal cortex.


• **Anosognosia is associated with decreased activation of the left medial prefrontal cortex.**

In England, 14 individuals with schizophrenia were subjected to functional magnetic resonance imaging (fMRI) both during an acute schizophrenia episode and again after they had been stabilized. During their fMRI, they were asked to do tasks which measured social functioning and awareness of illness. Their left medial prefrontal cortex showed improved activation when they were stabilized, and this correlated with improvement in insight scores (r=0.81, p<0.001).


• **Anosognosia is associated with decreased gray and white matter.**

At multiple sites in the United States and Europe, 251 individuals with first-episode psychosis were assessed for awareness of illness, using the ITAQ questionnaire, and for brain volume using MRI. Decreased whole brain volume, whole brain gray volume, and whole brain white volume were all statistically associated with decreased awareness of illness.


• **Anosognosia is associated with decreased volume of right dorsolateral prefrontal cortex and right orbitofrontal cortex.**
At the University of Texas Southwestern, 14 patients with schizophrenia and 21 normal controls were assessed for awareness of illness and symptoms and by magnetic resonance imaging (MRI). Patients with poorer awareness of their illness and symptoms also had significantly smaller right dorsolateral prefrontal cortex (r = -0.72, p = 0.04).


- **Anosognosia is associated with reduced gray matter in the cingulate and inferior temporal regions.**

In South Korea, 35 patients with paranoid schizophrenia and 35 matched normal controls underwent clinical testing and magnetic resonance imaging (MRI). Those with greater “lack of judgment and insight” had reduced gray matter in their right anterior cingulate, left posterior cingulate, and inferior temporal region on both sides.


- **Anosognosia is associated with decreased volume of the right dorsolateral prefrontal cortex.**

At the University of Pittsburgh, 35 individuals with first episode schizophrenia, who had never been treated with any antipsychotic drugs, were assessed clinically, neuropsychologically, and by magnetic resonance imaging (MRI) of the frontal lobes and hippocampus. 18 patients had poor awareness of their illness and 17 had good awareness of their illness. Those with poor awareness had decreased volumes of their right dorsolateral prefrontal cortex (DLPFC) (r = -61, p = 0.008). Unawareness of illness was not associated with hippocampal volume nor with duration of illness or other clinical symptoms.


- **Anosognosia is not correlated with global brain measures.**

In England, 78 men with schizophrenia and 36 normal controls were assessed for awareness of illness and underwent magnetic resonance imaging (MRI). There were “no significant correlations between total insight score and grey, white, CSF, and total brain volume.” The authors concluded that such research was not likely to be useful for such “global brain measures” and that “future investigations should pay attention to more specific cortical regions.”


- **Anosognosia is associated with specific subregions of the frontal lobes.**

At Dartmouth Medical School, 15 individuals with schizophrenia and schizoaffective disorder were assessed for awareness of illness and frontal brain structures by magnetic resonance imaging.
imaging (MRI). Those with less awareness of their illness had significantly smaller bilateral middle frontal gyrus volume ($r = -0.92$ and $-0.72$, $p<0.01$). There was also a trend for these individuals to have a smaller right gyrus rectus and left anterior cingulate gyrus. The authors concluded that “the strong correlations between bilateral middle frontal gyri and unawareness suggest involvement of dorsolateral prefrontal cortex,” an area that has been associated with schizophrenia in many neuropsychological and neuropathological studies.


- **Anosognosia is associated with atrophy of the frontal lobes.**

In Norway, 21 individuals with schizophrenia and 21 matched normal controls were assessed by computerized tomography (CT) scans. 7 of the 21 individuals with schizophrenia had mild or moderate atrophy of their frontal lobes, and this atrophy correlated with having poorer awareness of their illness ($r = -0.52$, $p<0.05$). Poorer awareness of illness also correlated with poorer executive function, a frontal lobe-associated trait, but not with other neuropsychological measures. The authors concluded that “unawareness of illness in schizophrenia may be related to frontal lobe deficit.”


- **Anosognosia is associated with having a smaller brain size.**

At Dartmouth Medical School, 18 individuals with schizophrenia with a poor awareness of their illness were compared on magnetic resonance imaging (MRI) with 12 individuals with schizophrenia with a good awareness of their illness and 13 healthy controls. There were no differences between the schizophrenia groups on education, symptoms, or severity of illness. However, those with poor awareness of their illness had significantly smaller brains and decreased intracranial volumes, findings consistent with having had a greater loss of brain tissue (atrophy) associated with their schizophrenia.


- **Anosognosia does not correlate with total ventricular volume.**

In England, 128 individuals with recent-onset psychosis were assessed for awareness of illness and underwent a computerized tomography (CT) scan. No correlation was found between awareness of illness and total ventricular volume.


- **Anosognosia correlates with enlarged brain ventricles.**
In Japan, 22 patients with chronic schizophrenia were assessed for awareness of illness and underwent magnetic resonance imaging (MRI). Those patients with impaired awareness of illness had significant ventricular enlargement (p<0.05).