BRIEF COMMUNICATION

Anosognosia and Alzheimer's Disease

Lorenzo Pia[1] and Paul M. Conway[2]

[1] *Department of Psychology and Neuropsychology Research Group, University of Turin, Italy*
[2] *Work Psychology Unit, Department of Occupational Health, University of Milan, Italy*

Neurological patients can be entirely unaware of their disease; this phenomenon is called anosognosia and it has been shown in different sensory-motor and cognitive domains. Lack of awareness has been investigated in Alzheimer's disease (AD) and within different domains of it. In the present article we review the literature on anosognosia for AD that had been indexed on the Medline database until the end of 2004. Historical introduction to the subject is followed by a brief description of the anatomy and clinical characteristics of AD. An analysis of a number of studies that focus on the relationship between anosognosia and AD then follows. This review shows that anosognosia is typical in AD, compared with other types of dementia, and it is a distinctive feature in the most severe cases and particularly in the beginning phases of illness. From an anatomical point of view, anosognosia seems to be strictly connected to frontal lobe areas; in fact, patients with anosognosia and AD show a reduction of cerebral haematic flow in the frontal regions, as well as deficits of executive functions and extrapyramidal signs. Interestingly, co-occurring depression could be interpreted as an adaptive behavior to counter the effects of perceived loss of cognitive abilities. Finally, self-awareness in AD could have some common mechanisms with auto-monitoring in schizophrenia.

Key words: anosognosia, unawareness, Alzheimer, lack of awareness, lack of insight

The first case of unawareness of a neurological disorder was reported by Seneca in Liber V, Epistula IX (Bisiach & Geminiani, 1991). Seneca described a woman who denied her blindness. Yet, the term 'anosognosia' has been introduced only in the 20th century by Babinski (Babinski, 1914). Until the beginning of the 20th century, anosognosia had been interpreted as a part of a more general disorder of body schema created and continuously modified by somatosensorial experiences (Head & Holmes, 1911). During the 1930s, based on Freudian theories, some authors suggested psychodynamic interpretations of anosognosia such that the lack of awareness could be a form of organic suppression (Schilder, 1932) or an avoidance reaction (Goldstein, 1939). The post-World War I period was characterised by discussion of the possibly significant role of motivations in the development of awareness. These so-called motivational theories presumed that premorbid components of personality were causally related to illness onset. These theories have their ancient roots in Charcot's demonstration of unawareness in patients without organic lesions (Charcot, 1892). Accordingly, during these years there was a decline of pure neurological approaches to the phenomenon (McGlynn & Schacter, 1989) in favor of more psychiatric perspectives (Prigatano & Schacter, 1991). From the 1960s, thanks to progress in cognitive neuroscience, in particular the demonstration of the selective occurrence of anosognosia, awareness again became an important phenomenon of study. Contemporarily, the motivational theories disappeared in favor of modular approaches that assumed a cognitive system organised in distinct components that are reciprocally connected. The most important prediction of such perspectives is

Address for correspondence: Lorenzo Pia, Ph.D, Department of Psychology and Neuropsychology Research Group, University of Turin, Via Po 14, 10123 Torino, Italy. E-mail: l_pia@psych.unito.it

that circumscribed lesions can produce very specific diseases, awareness disturbances included. Actually, many authors definitely agree in according domain specificity to anosognosia. That is, it may occur for one of the impaired domains but not for the others. Consequently, anosognosia has been reported for the sensory-motor domain as, for example, in anosognosia associated with Anton's syndrome, in hemianopia and in hemiplegia. On the other hand, it has been also observed in the cognitive domain, as in anosognosia for language deficits and for memory deficits, as well as in anosognosia in schizophrenia and in AD (see Giacino & Cicerone, 1998, for a review on the evolution of the concept of anosognosia and its different interpretations).

In AD and other types of dementia, anosognosia generally has not been considered as domain specific, and researchers have grouped data from different domains in a single anosognosia index (Antoine, Antoine, Guermonprez, & Frigard, 2004). However, recently, several studies have aimed to analyze more thoroughly the lack of awareness within AD.

Anatomy, Physiology and Clinical Characteristics of AD

On a macroscopic level, AD is characterised by a significant reduction of cerebral weight and by cortical atrophy, with a widening of the cerebral sulci and a leveling of the cerebral convolutions. On a microscopic level, the most relevant and distinctive lesional patterns are neuronal degeneration, congophilic angiopathy and, most of all, senile plaques and neurofibrillary degeneration. The brain regions most affected by such microscopic lesions are located mainly in the hippocampus, in the cingulate gyrus and in the associative areas (for an extensive review see Làdavas & Berti, 1999). The primary sensory specific areas are generally not affected and it is important to point out that AD results from multifocal lesions rather than a global degeneration of the cerebral tissue.

From a clinical point of view, the first evident symptoms are memory deficits, other instrumental function deficits and psychiatric disorders. Often, the first neuroradiologic examination is negative, while a confirmed diagnosis is possible only after postmortem examination. Nevertheless, a good diagnostic approximation can be reached through neuroradiologic evidence, in the presence of progressive memory deficits, in the absence of consciousness alterations and with illness onset included between 40 and 90 years of age (Làdavas & Berti, 1999).

AD and Anosognosia

Anosognosia is a particular feature of AD (McGlynn & Kaszniak, 1991) and it can present at the same or greater level of severity than the disease itself (Reisberg. Gordon, McCarthy, & Ferris, 1985; Starkstein, Chemerinski, Sabe, Kuzis, Petracca et al., 1997). Reisberg and colleagues (1985), for example, interviewed a group of patients with AD and memory deficits, by asking questions about their own functioning and that of their spouse. In the most severe cases of illness, AD patients tended to judge their own cognitive and behavioural abilities significantly better than objective measures; conversely, patients' opinions about their spouses' cognitive and behavioral integrity was corresponding to their spouses' opinions. Starkstein and colleagues (1997) in a longitudinal study on the development of anosognosia in AD, found a positive correlation between level of unawareness for cognitive functions and for daily activities, and illness severity. However, other workers did not report data consistent with these conclusions (Neary, Snowden, Bowen, Sims, Mann et al., 1986; Smith, Henderson, McCleary, Murdock, & Buckwalter, 2000). As regards the time course of the illness, anosognosia is more evident in acute phases of the disease; such a characteristic can be found also in Pick's disease (Fredericks, 1985; Gustafson & Nilsson, 1976). The two pathologies are associated with the typical signs of frontal damage, although those signs are less marked in AD. Hence, this distinction could be useful for differentiating AD from Pick's disease (Gustafson & Nilsson, 1976).

Many studies have reported attempts to test systematically the relationships between awareness for dementia and type of dementia. Danielczyk (1983), for instance, developed a clinical scale in order to evaluate insight for one's own condition. The scale was administered to four groups of patients affected by different disorders: Parkinson's disease, atypical Parkinson's disease with vascular signs, multi-infarct dementia and AD. Results showed anosognosia was more evident in AD than in atypical Parkinson and, finally, in multi-infarct dementia. Recently Tamietto and colleagues (Tamietto, Latini-Corazzini, Castelli & Geminiani, 2004) confirmed that anosognosia, particularly for memory deficits and daily abilities, is more frequent in AD than vascular dementia. Schacter and colleagues (Schater, McLachlan, Moscovitch, &

Tulving, 1986) tested patients' ability to predict their own performance in word recall and achieved similar results. That is, patients with AD overestimated their performance.

In the last 10 years, studies on anosognosia for AD focused their attention mainly on two aspects: the relationship between anosognosia and depression on the one hand, and the associations between unawareness of cognitive deficits and frontal lobe areas, on the other. With respect to the former topic, a crucial study was realized by means of clinical semistructured interviews for evaluation of the level of anosognosia for memory deficits (Sevush & Leve, 1993). Scores showed no correlation between anosognosia and age, educational level and length of illness; in contrast, a significant positive correlation was found between anosognosia and female gender as well as between anosognosia and presence of cognitive function deficits. The most important result of this study was the negative correlation found between awareness and depression: The more aware a person was, the more depressed this person became. Since during the recovery from illness patients become more and more aware of their disease, the authors concluded that depression, in this case, could be an adaptive reaction to the perception of losing a cognitive ability. The lack of correlation between anosognosia and length of illness suggests that Alzheimer's patients did not become aware of their condition, despite prolonged exposure to their illness and to repeated feedback by family and doctors.

Another study found a relation between unawareness for cognitive deficits and the Hamilton Depression Scale (Hamilton, 1967). Specifically, the scores of this scale were significantly correlated to the degree of unawareness. In other words, the more a patient was unaware of his/her cognitive deficits the less depressed he/she was (Starkstein, Sabe, Chemerinski, Jason, & Leiguarda, 1996). These data confirm the results of Sevush and Leve's (1993) study, further supporting the crucial role of depression in this kind of anosognosia. In a subsequent study, Starkstein et al. (1997) further examined these correlations through study of the longitudinal evolution of depression and anosognosia. They confirmed the above-mentioned negative correlation. However, this was true only for major depression but not for dysthymia. Further, Smith et al. (2000) showed that higher levels of anosognosia are associated with lower performance on specific cognitive tasks. Thus, depressive symptoms may confound the relationship between anosognosia and dementia severity. Almeida and Crocco (2000) analysed these possible confounding factors. They reported that lack of awareness for cognitive and behavioral deficits in AD was not influenced by the presence of depressive symptoms.

With respect to the other aforementioned topic of research during the last 10 years, namely the relationship between frontal lobe deficits and awareness of cognitive deficits, most of the studies have used different tests to evaluate cognitive functions as well as different questionnaires to evaluate self-awareness. A general correlation between the compromising of executive functions, typically attributed to frontal areas, and the level of anosognosia for memory deficits and for dementia severity has been observed regularly (Lopez, Beker, Somsak, Dew, & DeKosky, 1994; Michon, Deweer, Pillon, Agid, & Dubois, 1994;). Lopez and colleagues (1994) interpreted this correlation by proposing that executive functions could be synthesised within the concept of the Central Executive System (CES) component of Working Memory (Baddeley, 1986) that coordinates attention and information flow to and from verbal and spatial short-term memory slave systems.

The CES shares some common features with Stuss and Benson's (1986) executive system. However, the CES implies the interaction between memory, language, abstract thought and visual–spatial abilities as well. Any damage to the CES produces a dysexecutive syndrome and can cause symptoms similar to those associated with frontal lesions. Such a syndrome can be observed from the beginning of dementia. Lopez et al. (1994) suggested that, in these patients, anosognosia follows damage to the CES. In 1995, Dalla Barba and coworkers (Dalla Barba, Parlato, Iavarone, & Boller, 1995) pointed out that while frontal functions had been shown to play a relevant role in anosognosia for memory deficits in AD, they had not been shown to be a necessary condition.

The relationship between frontal lobe functions and awareness in patients with AD has been confirmed also with radiological and anatomical examinations. Patients with AD and anosognosia showed a reduction of cerebral haematic flow in right frontal regions (Reed, Jagust, & Coulter, 1993; Starkstein et al., 1995), and this reduction seemed to be larger with more severe anosognosia (Starkstein et al. 1995). Starkstein et al. (1997) showed that in patients with severe anosognosia, extrapyramidal signs are more marked. Taking into account these results and the fact that patients with those signs showed more severe deficits in frontal tasks compared to patients without such signs (Merello, Sabe, & Teson, 1994), it has been proposed that the frontal dysfunction causes the

anosognosia and other specific cognitive deficits in AD (Starkstein et al., 1997). Regarding the anatomical-clinical correlation, the aforementioned Sevush and Leve's (1993) study reported different data. Indeed, they found a negative correlation between unawareness of memory disorders and a specific test for object naming that might have a specific neural basis. In fact, Strub and Black (1988) showed that lesions to the temporal inferior dominant lobe, confined to Brodmann's area 37 could produce isolated disorders of object naming. Thus, damage to areas adjacent to frontal lobes might be partly responsible for the denial of memory deficit in AD.

Interestingly, in a different research field, some authors have reported results that may shed further light on the relationships between awareness and AD. Certain data show common cerebral dysfunctions between schizophrenia and dementia with frontal lobe atrophy (McGlynn & Kaszniak, 1991) on the one hand, and common deficits between schizophrenia and dementia in tests for frontal or executive functions on the other (Kolb & Whishaw, 1983). These data reinforce the idea of a close relationship between unawareness in schizophrenia and frontal lobe dysfunction. Thus, it has been proposed that anosognosia within AD could be a consequence of damage to the executive functions supported by prefrontal areas (Mohamed, Fleming, Penn, & Spaulding, 1999; Young, Zakzanis, Bailey, Davila, Griese et al., 1998). Such supposition can lead us to think about a similarity with those mechanisms responsible for auto-monitoring deficits in dementia.

Conclusions

Despite the dramatic disabling nature of impairment, many patients are completely unaware of their own neurological disease; this phenomenon is known as anosognosia. This phenomenon makes rehabilitation more difficult and is a negative prognostic factor for recovery. Conversely, it may provide us with many important hints for understanding the monitoring process of our own conditions, disclosing implicit mental contents, and shedding light on the neural structures underlying conscious mental processes. Research on AD has addressed anosognosia in the early stages of the disease and across different aspects of functioning including cognition, mood, behavior and daily activities. In this paper, we considered the literature on anosognosia in AD and attempted to synthesise important clinical and anatomical research findings. For a long time anosognosia in AD has been described as a symptom, without further specifying its own etiological nature. Nevertheless, recent findings seem to suggest an interesting possibility, namely that unawareness in schizophrenia might be interpreted as a neurologically based condition. Our review can be summarised in the following points: (1) Anosognosia in AD might occur as a neurological disorder per se due to frontal lobe damage (Goldberg & Costa, 1986; Kolb & Whishaw, 1983; Lopez et al., 1994; McGlynn & Kaszniak, 1991; Michon et al., 1994; Reed et al., 1993; Starkstein et al., 1995; Starkstein, Sabe, Chemerinski, Jason, & Leiguardaa, 1996; Starkstein et al., 1997); (2) Anosognosia in AD might occur *in* the illness as a whole or *within* different domains of it; (3) Anosognosia in AD is peculiar to the beginning phases of the illness (Fredericks, 1985; Gustafson & Nilsson, 1976); and (4) it is positively correlated to the severity of the diagnostic picture (Reisberg et al., 1985; Starkstein et al., 1997).

In summary, the possible existence of a pure neurologically based form of unawareness within AD, is not yet definitive and unquestionable. Here we have tried to stress the importance of deepening consideration of the neurological basis of unawareness as well as its possible manifestation as a domain-specific phenomenon. This should allow clarification of the role of defensive mechanisms or general mental deterioration and a more satisfying anatomical-functional picture of anosognosia. Since anosognosia is a poor prognostic factor for functional recovery, understanding its etiology and its relationship with the neurocognitive system is imperative in order to tailor and manage treatment accordingly. To conclude, we hope that this review can contribute to encourage further studies as well as theoretical discussions on this interesting topic.

Acknowledgments

This work was supported by a grant from the Royal Society and by one from the Piedmont Region to Lorenzo Pia.

References

Almeida, O.P., & Crocco, E.I. (2000). Perception of cognitive deficits and behavior disorders in patients with AD. *Arquivos de Neuro-psiquiatria*, *58*, 292–299.

Antoine, C., Antoine, P., Guermonprez, P., & Frigard B. (2004). Awareness of deficits and anosognosia in AD. *Encephale*, *30*(6), 570–757.

Babinski, J. (1914). Contribution à létude des troubles mentaux dans l'hémiplégie organique cérébrale (anosognosie). *Revue Neurologique*, *27*, 845–848.

Baddeley, A.D. (1986). *Working memory*. London: Oxford University Press.

Bisiach, E. & Geminiani, G. (1991). Anosognosia related to hemiplegia and hemianopia. In G.P. Prigatano & D.L. Schacter (Eds.). *Awareness of deficit after brain injury* (pp. 17–39). New York: Oxford University Press.

Charcot, J. M. (1892). *Lecons du Mardi à la Salpetrière: Policlinique*, (2nd ed., 1887–1888). Paris: Louis Battaille.

Dalla Barba, G., Parlato, V., Iavarone, A., & Boller F. (1995). Anosognosia, intrusions and 'frontal' functions in Alzheimer disease and depression. *Neuropsychologia*, *33*, 247–259.

Danielczyk, W. (1983). Various mental behavioral disorders in Parkinson's disease, primary degenerative senile dementia, and multiple infarction dementia. *Journal of Neural Transmission*, *56*, 161–176.

Fredericks, J.A.M. (Ed.). (1985). The neurology of aging and dementia. *Handbook of clinical neurology* (pp. 199–219). Amsterdam: Elsevier.

Giacino, J.T., & Cicerone, K.D. (1998). Varieties of unawareness of deficits after brain injury. *Journal of Head Trauma Rehabilitation*, *13*(5), 1–15.

Goldberg, E., & Costa, L.D. (1986). Qualitative indices in neuropsychological assessment: An extension of Luria's approach to executive deficit following prefrontal lesions. In J. Grant & K.M. Adams (Eds.), *Neuropsychological assessment of neuropsychiatric disorders* (pp. 147–171). New York: Oxford University Press.

Goldstein, K. (1939). *The organism: A holistic approach to biology derived from pathological data on man*. New York: American Book Co.

Gustafson, I., & Nilsson, L. (1982). Differential diagnosis of presenile dementia on clinical grounds. *Acta Psychiatrica Scandinavica*, *65*, 194–207.

Hamilton, M. (1967). Development of a rating scale for primary depressive illness. *The British Journal of Social and Clinical Psychology*, *6*, 278–296.

Head, H., & Holmes, J. (1911). Sensory disturbances from cerebral lesions. *Brain*, *34*, 102–254.

Kolb, B., & Whishaw, I.Q. (1983). Performance of schizophrenic patients on tests sensitive to left or right frontal, temporal, or parietal function in neurological patients. *Journal of Nervous and Mental Disease*, *171*, 435–443.

Làdavas, E., & Berti, A. (1999). *Neuropsicologia.* Bologna, Italy: Il Mulino.

Lopez, O.L., Beker, J.T., Somsak, D., Dew, M.A., & DeKosky, S. (1994). Awareness of cognitive deficits and anosognosia in probable AD. *European Neurology*, *34*, 277–282.

McGlynn, S.M., & Kaszniak, A.W. (1991). Unawareness of deficit in dementia and schizophrenia. In G.P. Prigatano & D.L. Schacter (Eds.), *Awareness of deficit after brain injury* (pp. 84–110). New York: Oxford University Press.

McGlynn, S.M., & Schacter, D.L. (1989). Unawareness of deficits in neuropsychological syndromes. *Journal of Clinical and Experimental Neuropsychology*, *11*, 143–205.

Merello, M., Sabe, L., & Teson, A. (1994). Extrapyramidalism in AD: Prevalence, psychiatric and neuropsychological correlates. *Journal of Neurology, Neurosurgery and Psychiatry*, *57*, 1103–1110.

Michon, A., Deweer, B., Pillon, B., Agid, Y., & Dubois, B. (1994). Relation of anosognosia to frontal lobe dysfunction in AD. *Journal of Neurology, Neurosurgery, and Psychiatry*, *57*, 805–809.

Mohamed, S., Fleming, S., Penn, D. L., & Spaulding, W. (1999). Insight in schizophrenia: Its relationship to measures of executive functions. *Journal of Nervous and Mental Disease*, *187*, 525–531.

Neary, D., Snowden, J.S., Bowen, J.S., Sims, N.R., Mann, D.M.A., Benton, J.S et al. (1986). Neuropsychological syndromes in presenile dementia due to cerebral atrophy. *Journal of Neurology, Neurosurgery and Psychiatry*, *49*, 163–174.

Prigatano, G.P., & Schacter, D.L. (1991). Awareness of deficit after brain injury. In G.P. Prigatano & D.L. Schacter (Eds), *Awareness of deficit after brain injury* (pp. 3–16). New York: Oxford University Press.

Reed, B.R., Jagust, W.J., & Coulter, L. (1993). Anosognosia in AD: Relationship to depression, cognitive function, and cerebral perfusion. *Journal of Clinical and Experimental Neuropsychology*, *15*, 231–244.

Reisberg, B., Gordon, B., McCarthy, M., & Ferris, S. H. (1985). Clinical symptoms accompanying progressive cognitive decline and AD. In V. L. Melnick & N.N. Dubler (Eds.), *Alzheimer's dementia* (pp. 19–39). Clifton: Humana Press.

Schacter, D.L., McLachlan, D.R., Moscovitch, M., & Tulving, E. (1986). Monitoring of recall performance by memory-disordered patients. *Journal of Clinical and Experimental Neuropsychology*, *8*, 130.

Schilder P. (1932). Localization of the body image (postural model of the body). *Association for Research in Nervous and Mental Disorders*, *13*, 466–484.

Sevush, S., & Leve, N. (1993). Denial of memory deficit in AD. *American Journal of Psychiatry*, *150*, 748–751.

Smith, C. A., Henderson, V. W., McCleary, C. A., Murdock, G. A., & Buckwalter, J. G. (2000). Anosognosia and AD: The role of depressive symptoms in mediating impaired insight. *Journal of Clinical and Experimental Neuropsychology*, *22*(4), 437–44.

Starkstein, S., Chemerinski, E., Sabe, L., Kuzis, G., Petracca, G., Teson, A. et al. (1997). Prospective longitudinal study of depression and anosognosia in AD. *British Journal of Psychiatry*, *171*, 47–52.

Starkstein, S., Sabe, L., Chemerinski, E., Jason, L., & Leiguarda, R. (1996). Two domains of anosagnosia in AD. *Journal of Neurology, Neurosurgery and Psychiatry*, *61*, 485–490.

Starkstein, S.E., Vazquez, S., Migliorelli, R., Teson, A., Sabe, L., & Leiguarda, R. (1995). A single-photon emission computed tomographic study of anosognosia in AD. *Archives of Neurology*, *52* 415–420.

Strub, R.L., & Black, W.F. (Eds.). (1988). *Neurobehavioral disorders: A clinical approach.* Philadelphia: Davis.

Stuss, D.T., & Benson, D.F. (1986). *The frontal lobes*. New York: Raven Press.

Tamietto, M., Latini-Corazzini, L., Castelli, L., & Geminiani, G. (2004). Domain-specific anosognosia in AD and vascular dementia. *Brain Impairment, 5,* 187–197.

Young, D.A., Zakzanis, K.K., Bailey, C., Davila, R., Griese, J., Sartory, G. et al. (1998). Further parameters of insight and neuropsychological deficit in schizophrenia and other chronic mental disease. *Journal of Nervous and Mental Disease*, *186*, 44–50.