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Front Temporal Dementia and Imputability

The Role of Forensic Neurosciences in the Ability to Understand and Want

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INTRODUCTION

In all forms of dementia, neuropsychiatric symptoms are present alongside cognitive ones. For a long time, the latter have been considered characteristic of dementias, and only since 2011 has their presence been recognized as a distinctive clinical element.[1]

In the new criteria proposed by the National Institute on Aging and the Alzheimer Association, dementia is diagnosed when there are "cognitive or neuropsychiatric symptoms that interfere with the ability to perform work or usual activities and represent a decline from previous levels of functioning and performance, not explained by delirium or major psychiatric disorders".[2]

The evaluation of neuropsychiatric symptoms represents a focus in the approach to the patient with dementia, both for their relevance from the diagnostic point of view, for the impact on the quality of life of the patient and the family, and also because they constitute one of the outcomes of the therapeutic intervention (pharmacological and non-pharmacological) of dementia.[3]

The presence of neuropsychiatric symptoms [hereinafter N.P.S.] involves an increase in the risk of early institutionalization, with the same neurological severity of dementia, it causes extreme disability and worse cognitive performance, a reduction in the quality of life of patients and caregivers, a significant increase in social costs and stress for the caregiver.[4]

The definition and characterization of non-cognitive symptoms, as well as the appropriate methodology and assessment tools when diagnosing, are still a subject of debate. It is a symptom complex that is not easily characterized in a homogeneous way; for a long time, the generic expression "non-cognitive symptoms" was used to define everything that appeared different from the nucleus or syndrome considered central in dementia. In 1996, the Consensus Conference of the International Psychogeriatric Association [hereinafter I.P.A.] published a definition of these symptoms, promoting the term Behavioral and Psychological Symptoms of Dementia [hereinafter B.P.S.D.]. According to the I.P.A., "the term behavioral disturbances should be replaced with that of behavioral and psychological symptoms of dementia (B.P.S.D.) defined as: symptoms of

[1] Guy M. McKhann et al., *The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease*, 7 The J. Alzheimer's Ass'n 263 (2011).

[2] Angelo Bianchetti et al., *I nuovi criteri per la diagnosi di demenza e di Mild Cognitive Impairment dovuti alla malattia di Alzheimer* [*The new criteria for a dementia and Mild Cognitive Impairment diagnosis due to Alzheimer's disease*], 2 Associazione Italiana Psicogeriatria [Italian Ass'n Psychogeriatrics] 90 (2011) (Ita.).

[3] Helen C. Kales et al., *Assessment and management of behavioral and psychological symptoms of dementia*, 350 Brit. Med. J. (2015).

[4] Renzo Rozzini et al., Medicina della fragilità. Manuale di Lavoro [Medicine of Frailty. Working Manual] 189-2013 (2014).

altered perception, thought content, mood of behavior frequently present in patients with dementia".[5] These symptoms are grouped according to the frequency and level of stress caused and complexity in management.[6]

2. DEMENTIA WITH BEHAVIORAL DISORDERS

We have just seen that all dementias present behavioral disturbances in their syndromic procession. There are, however, some that, more than others, have behavioral disorders at onset as their gold standard. Among them we have the family of fronto-temporal dementias, which, together with Lewy body dementia and frontal variant Alzheimer's dementia, are those with an elective self-presence with neuropsychiatric symptoms, followed by vascular dementia (Va.D.) and from substance abuse dementia (alcohol and drugs).

This is because the frontal lobe is involved and the circuitry that, from it, leads to the nuclei of the base, in particular to the caudate nucleus. This circuitry is involved in the ability to self-control. Since it is the first to deteriorate in these forms of dementia, often the patient who is affected by this disease comes to the attention of a psychiatrist before a neurologist is consulted. It is not infrequent that these patients are treated for extended periods, even years, in psychiatric institutions, demonstrating a poor response to psychotherapeutic treatments, until the appearance of cognitive deficits leads these patients to a neurologist. They are the kind of patients who, in their medical history, might have, at the onset of the disease, some criminal proceedings for minor crimes that they would never have committed, a sign of a change in character. The writer remembers having diagnosed fronto-temporal dementia, a behavioral variant, in a seventy-five-year-old lady, who was the recipient of a summons for stealing a low-value lipstick (€2.90) at the supermarket, an action that she would never have purposely executed and that had negative consequences on her family as well.

The lady, apparently well-kempt and still in order in terms of clothing and self-care, nevertheless showed a kind of trivialization of the problem, which she did not understand. She was not at all aware of having to undergo a criminal trial for theft, and this alerted the writer who, instead of limiting himself to a basic neurological vision, spent time performing neuropsychological tests, from which the impairment of the functions underlying the frontal lobe, such as the ability to criticize and judge, to plan and to solve problems, clearly emerged.

[5] Sanford I. Finkel et al., *Behavioral and psychological signs and symptoms of dementia: a consensus statement on current knowledge and implications for research and treatment*, 8 Int'l Psychogeriatrcis 497 (1996).

[6] *See* International Psychogeriatric Association, *Better Mental Health for Older People* http://www.ipa-online.org (last visited Feb. 13, 2022).

At that point, as a first action, I advised a morpho-volumetric Magnetic resonance imaging [hereinafter M.R.I.], of the second and third level tests, and I entrusted it to a good criminal lawyer, who was able to ask for an expert opinion from which emerged his inability to understand and decide for himself, for a frontal dementia-temporal, electively behavioral variant, of intermediate degree. The M.R.I. images, in fact, allowed to demonstrate a severe atrophy of the left frontal lobe, consistent with the tests, which also showed a language deficit.

3. DEMENTIA AND IMPUTABILITY

One of the most complex questions to answer, and much debated, is the following, well expressed by the title of an article that I propose to the reader: "When can a person with dementia be held liable for her actions?".[7]

The relatively recent data gives us the measure of how much this problem is relevant, not only in the civil field but, also and above all, in the criminal field, where responsibility is personal.

This article proposes, for example, two problem questions in the civil field, which are useful for a reflection on the criminal one as well. Here are the two scenarios and their solutions:

- Case 1: Lisa G. is suffering from dementia, lives in a nursing home and has spilled paint on the parquet floor. In an attempt to remove the stains with unsuitable products, she damaged the parquet. Does she have to pay for the damage herself and pay for the repair work? The civil liability insurance found that Lisa G. was not required to compensate for the damage caused as she was unable to discern. Consequently, the insurance company is not obliged to do so either. Consequently, the health care institution that suffered the damage had to bear the costs. The family would have preferred the liability insurance to pay for the damage, as Lisa G. has been paying premiums for years.

- Case 2: Margrit K. has dementia and still lives at home alone. She wrongly disposed of her waste bags, and the municipality imposed a 150 franc fine on her. Her son challenged it in front of the competent court. The latter ruled that in these situations, it is very likely to have a lack of imputability or reduced imputability.

[7] Sanford I. Finkel et al., *Behavioral and Psychological Signs and Symptoms of Dementia: Implications for Research and Treatment,* 8 Int'l Psychogeriatrics 497 (1997). Quando una persona affetta da demenza può essere ritenuta responsabile? [When can a person with dementia be held liable for her actions?], Auguste, Alzheimer Schweiz [Alzheimer Switzerland], April 2019, https://www.alzheimer-schweiz.ch/it/auguste/diritto/detail/quando-una-persona-affetta-da-demenza-puo-essere-ritenuta-responsabile.

The case must be reviewed by the court of first instance. If, due to dementia, Margrit K. was no longer able to judge which garbage bag was to be used, she is not liable. In that case the sentence would have been revoked. The article concludes in this way:

> Both cases show that a diagnosis of dementia does not automatically equate to an inability to discern. Many factors play a role. It is often difficult to determine whether or not the person concerned is incapable of discernment or imputable in the concrete situation. However, if you are not aware of the consequences of your actions, you cannot under any circumstances be held responsible [t/n original article in German, French and Italian].

Therefore, the question is when, and by what means, can a person with dementia be considered aware or not of the consequences of their actions, or capable of "understanding" pursuant to art. 85 of the Italian Criminal Code?

The answer is very complex and cannot ignore an important consideration: there is no single type of dementia; instead, there is a vast variety of forms of dementia, due to different etiopathogenesis and different neuronal networks involved.

Once, Alois Alzheimer identified the "Queen" of dementias by means of an anatomo-clinical correlation between the memory defect (or, better, of the different forms of memory) and an atrophy in a particular brain area (the hippocampus, seat of our ability to memorize). In later times, sophisticated work of study and classification has made it possible to identify alternative forms of dementia, some of which do not necessarily entail a loss of memory. However , they are no less relevant from the point of view of imputability, as they affect areas (such as the frontal lobes) which are the seat of our capacity for criticism and judgment, as well as for impulse control and of our inner needs.Therefore, a complete answer to this question must consider the different forms of dementia known today, their evolutionary fate, and the consequences of it on the side of so-called behavioral disorders (B.P.S.D.).

4. BEHAVIORAL DISORDERS IN DEMENTIA

Let's start by considering the field of behavioral disorders, a real problem that underlies the evaluation of a demented patient's ability to understand and / or want.

Internationally, behavioral disorders have been defined as "alterations in perception, thought content, mood or behavior, which are frequently observed

in patients with dementia".[8]

The term, "behavioral and psychological symptoms of dementia" (B.P.S.D.), is intended to function as an "umbrella" term, covering various paroxysmal manifestations, and not necessarily as a definition of a specific clinical condition.[9]

What we must immediately bear in mind is this fact: 90% of people with dementia will experience cognitive behavioral symptoms during their illness, which are severe enough to become a problem on their own.[10]

They are symptoms of dementia, identified by Alzheimer's himself, and appear at any stage of dementia.[11]

We must also bear in mind that their severity is independent of the severity of the disease. Put simply, the severity of these disorders does not correlate with cognitive impairment (memory impairment and other higher cortical functions), which is why it can happen (and this is to be borne in mind in the criminal context) that a patient with an apparently mild (only from a cognitive point of view) dementia, is already in the throes of a severe behavioral disorder.

It happens, as we will see later when we will mention the different forms of dementia, in those so-called "frontal" forms of dementia (the "frontal-temporal dementias" or the "front-front" variant of Alzheimer's dementia), where the peculiar stigmata is precisely the dis-control of impulses, and the inability to resist a provocation, with a reaction that is often uncontrolled and disproportionate to the stimulus.

A characteristic aspect of behavioral disorders, beyond the fact that they are seen in all forms and stages of dementia , is their probable correlation with some types of dementia. In Alzheimer's, it seems that delusions and hallucinations may predominate; in Lewv body dementia, we can find aggressive behavior and hallucinations, especially visual; in the fronto-temporal dementias, as mentioned before, we can encounter delusions and disturbances of social conduct, with the appearance of abilities;[12] in dementia secondary to Huntington's chorea (which always affects the frontal and fronto-caudal network) we can see early onset depression with later psychotic

[8] Sanford I. Finkel & Alistair Burns, *Behavioral and Psychological Symptoms of Dementia: A Clinical and Research Update,* 12 Int'l Psychogeriatrics 9 (2000). Behavioral and Psychological Signs and Symptoms of Dementia: Implications for Research and Treatment, Proceedings of an international consensus conference held in Lansdowne, Virginia (April, 1996), *in* 8 International Psychogeriatrics 1996, at Suppl. 3:215-552.

[9] *See* S. I. Finkel and A. Burns, *Behavioral and Psychological Symptoms of Dementia (BPSD): a clinical and research update*, 12 International Psychogeriatrics (2000); 9–12.

[10] *See* I.P.A's update of 2000.Michael S. Mega et al., *The Spectrum of Behavioral Changes in Alzheimer's Disease,* 46 Neurology 130 (1996).

[11] *See, e.g.*, B. Reisberg et al., *The stage specific temporal course of Alzheimer's disease: functional and behavioural concomitants upon cross-sectional and longitudinal observation.* in review. prog. clin biol res 1989; 317: 23-41.

[12] *See, e.g.*, Sonia Rosso et al., *Complex compulsive behaviour in the temporal variant of frontotemporal dementia*, 248 J. Neurology 965 (2001) ; Bruce Cumming et al., *Cortical Area MT and the Perception of Stereoscopic Depth*, 394 Nature 677 (1998).

disorders;[13] finally, in vascular dementia, we can find emotional instability, agitation or apathy (depending on the site affected by the cerebral stroke, be it ischemic or hemorrhagic).

In all cases, behavioral disorders are the cause of severe stress on caregivers,[14] the most frequent cause of medical intervention, drug prescription, and even institutionalization.[15]

They cause a reduced quality of life of the patient and the caregiver,[16] increase in disability,[17] increase in the economic costs of disease.[18] The last problem also includes possible compensation for damages (pursuant to articles 2043-2059 of the Italian Civil Code) if the patient is not correctly studied in the entirety of his disorder, and is thus wrongly held capable of understanding and / or wanting.

5. CLASSIFICATION B.P.S.D.

More recently, a working group of the International Society to Advance Alzheimer's Research [hereinafter I.S.T.A.A.R.T.] and Treatment (Neuropsychiatric Syndromes Professional Interest Area (N.P.S.-P.I.A.) of I.S.T.A.A.R.T.) has produced a series of recommendations and among these the use of the term "neuropsychiatric symptoms of dementia" (neuropsychiatric symptoms (N.P.S.) grouping them into five clusters (in decreasing order of prevalence): depression, apathy, sleep disturbances, agitation and psychosis.[19]

To try to classify behavioral, or neuropsychiatric, disorders, we can bear in mind that they fall into two broad categories: altered behavioral symptoms and altered psychological symptoms.

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[13] J.L.Cummings, Behavioural and psychiatric symptoms associated with Hungtington's disease, Adv Neurol (1995); 65:179-186.

[14] *See* J.L. Cummings ., *Behavioural and psychiatric symptoms associated with Hungtington's disease*, Adv Neurol (1995).

[15] *See generally* Elizabeth J. Colerick & Linda K. George, *Predictors of Institutionalization among Caregivers of Patients with Alzheimer's Disease*, 34 J. Am. Geriatrics Soc'y 493 (1986). Neil Morris & Dylan M. Jones, *Memory Updating in Working Memory: The Role of the Central Executive*, 81 Brit. J. Psych. 111 (1990); Steele et al., *Alcol myopia: Its prized and dangerous effects*, in American Psychologist 1990, 45(8), 921-933; B.F. O' Donnell et al., *Incontinence and troublesome behaviors predict institutionalization in dementia,* 5 Journal of Geriatric Psychiatry and Neurology 45 (1992).

[16] *See* Gary T. Deimling & David M. Bass, *Symptoms of Mental Impairment Among Elderly Adults and Their Effects on Family Caregivers*, 41 J. Gerontology 778 (1986); *see also* M.S. Bourgeois et al., *When Primary and Secondary Caregivers Disagree: Predictors and Psychosocial Consequences*, 11 Psychol. & Aging 527 (1996).

[17] *See* E.B. Brody, *Are We for Mental Health As Well As Against Mental Illness? The Significance for Psychiatry of a Global Mental Health Coalition*, 139 Am. J. Psychiatry 1588 (1982).

[18] *See* Jiska Cohen-Mansfield, *Stress in Nursing Home Staff: A Review and a Theoretical Model*, 14 J. Applied Gerontology 444 (1995).

[19] *See* Yonas E. Geda et al., *Neuropsychiatric Symptoms in Alzheimer's Disease: Past Progress and Anticipation of the Future*, 9 Alzheimer's & Dementia 602 (2013).

Altered behavioral symptoms are usually identified by observation of the patient, and include aggression, yelling, continuous movement, agitation, sexual disinhibition, culturally inappropriate behavior, hoarding, swearing and stalking.

Altered psychological symptoms, usually and mainly assessed on the basis of interviews with patients and relatives, include anxiety, depressive mood, hallucinations and delusions.

It is important to mention their prevalence, or the number of cases in the general population. Since it is a chronic disease, in patients with delayed diagnosis (with rare exceptions such as dementia in Creutzfeldt Jakob spongiform encephalopathy) for several years, the prevalence is quite high.[20]

6. FREQUENCY

N.P.S. (meaning "neuropsychiatric symptoms") tend to be fluctuating and their persistence throughout the course of dementia (especially in Alzheimer's disease) can be variable. Depression and anxiety have a prevalence of 60% at two years, delusions and hallucinations tend to have a lower persistence (in 30% of cases it is present for the course of the disease), agitation, irritability and wandering tend to be more persistent (about 80% at two years of observation), apathy is the symptom with greater prevalence and persistence over time.[21]

Delirium has a frequency between 10 and 37% depending on the studies.[22] The most frequent forms are the delusion of persecution and paranoia,[23] but there are others. There are practically five most frequent delusions:I) delusion of theft (most common); the patient hides things and does not remember where he has placed them; in the most serious cases, he believes that people enter the house to steal what, in reality, they have lost; II)delusion of loss; the patient does not recognize his home as he remembers that of his childhood; a desire to return to a childhood home is present even years after first institutionalization; III) the spouse or caregiver is an impostor (Capgras phenomenon); IV) delirium of abandonment; the patient believes there is a conspiracy to institutionalize or abandon him; V)delusion of infidelity, sexual or otherwise, on the part of the spouse; the patient believes he is betrayed.

We must bear in mind, and this is especially relevant for lawyers who defend a suspect suspected of dementia and judges who decide those cases, that the delusion can

[20] *See* Cohen GD & Bergen M Hasegawa K, *Finkel SI Psychogeriatrics in the 1990's*, Int Psychogeriatr. (1990) Spring; 2(1): 7-8.
[21] *See* Rianne M. van der Linde et al., *Longitudinal Course of Behavioural and Psychological Symptoms of Dementia: Systematic Review*, 209 Brit. J. Psychiatry 366 (2016).
[22] *See* R.E. Wragg et al., *Overview of Depression and Psychosis in Alzheimer's Disease*, 146 Am. J. Psychiatry 577 (1989).
[23] *See supra* note 15, Morris.

lead to aggression, not always desired or controllable by the patient. To this end, I recall an example, a clinical case in which I was asked for a report by the judge of the criminal court of Verona, on a patient in a nursing home in eastern Verona. One evening, tired of hearing her roommate (also demented) scream, she got up in a delirium of thievery (she thought she had thieves in the house) and crushed her forehead and nose with a chair. The police officers intervened, reported to the Verona Public Prosecutor's Office, and the patient was served a summons for serious personal injury. Since she was only transportable in a wheelchair and was in a state of very serious dementia (she was not even aware of what she had done), the judge immediately deemed necessary, rather than an expert opinion, a report by the neurologist who followed her for dementia, given previous relationships exhibited by family members.

The patient, clearly incapable of understanding and willing, was declared not only unable to stand trial but not attributable pursuant to art. 85 of the Italian Criminal Code. In this case, the patient was also very cognitively impaired but, as we have already said, the opposite can also happen, namely that the behavioral disorder is the onset indicator of dementia, when the cognitive aspect still seems to be preserved.

This is why, in approaching the examination of imputability, one must always keep in mind, alongside the purely psychiatric aspect, the neurological-organic aspect of the behavioral disorder.

Among other symptoms, we have hallucinations, with a frequency ranging from 14 to 29%. The most frequent are visual ones and occur in moderate dementia.[24] They increase markedly, so much so that they become one of the diagnostic criteria in Lewy body dementia, where they settle on a frequency of 80%.

The most frequent form is to see people who are not there. In some cases, these hallucinations can generate agitation, and in this case they must be treated. The origin seems to be the difficulty in recognizing faces or objects (visual agnosia or prosopagnosia) associated with difficulty in distinguishing light-dark contrasts. It is advisable that each patient is assessed on the visual ability and that the environments are adequately illuminated in order to reduce visual hallucinations.

Then we have the misidentifications. They are disorders in perception. Unlike delusions, which do not follow an external stimulus, misidentifications are alterations in the perception, or misperceptions, of external stimuli that are processed until they become real delusions.

Misidentifications can be of four types: presence of people in the house or ghost tenant syndrome, inability to recognize oneself in the mirror, inability to recognize

[24] *See* Carol F. Lippa et al., *Alzheimer's Disease and Lewy Body Disease: A Comparative Clinicopathological Study,* 35 Annals Neurology 81 (1994).

other people, inability to recognize what is happening on the T.V. with the belief that people seen on T.V. are present in real space. We then have particular syndromes. Capgras or impostor syndrome, which makes one believe that a person has been replaced by an identical copy, is associated with the lack of affective signs and this leads the patient to the conclusion that the person is an impostor. Fregoli syndrome makes people believe that they dress like different people in order not to be recognised by others. There is also inter-metamorphosis, whereby the physical appearance of one person corresponds to that of another.

Depression affects 40-50% of patients. While in the initial forms of dementia the diagnosis can be made during an interview, in the more advanced stages of dementia, language and communication difficulties make it even more challenging.

Apathy affects about 50% of the demented. It manifests itself as a loss of interest in daily activities and personal care. It can be confused with major depression, but unlike in case of the latter, the patientdoes not have dysphoria and typical vegetative symptoms.

Anxiety can be isolated or linked to other Borderline Personality Disorders (B.P.D.s). It manifests itself with anxiety about finances, illness, and the future. The most common manifestation is Godot syndrome, in which the patient repeatedly asks about an event that is about to take place. Another form is the fear of being alone, especially when the cohabiting caregiver leaves the room in which the patient is for short moments. Then we have the phenomenon called wandering (or Wandering) which is particularly tiring for the caregiver. This term includes the continuous search of the caregiver, the stalking, walking, trying ineffectively to perform a task, and walking without purpose, often associated with the alteration of the sleep-wake rhythm, as well as hyperactivity, the attempt to return to a childhood home, and escape attempts from the care facility.

Agitation is defined as inappropriate verbal, vocal or motoric activity that does not result from a person's needs or confusion.[25] It is a sign and symptom of lack of comfort or discontent and puts the patient at risk of fracture. But not all agitation should be treated pharmacologically, and, when treated, it is necessary to be clear about what triggered it (one counts as an agitation due to a state of anxiety, as a delirium, another as an agitation due to a depressive syndrome). Above all, certain drugs (such as benzodiazepines) should be avoided, to avoid the so-called "paradox effect" (accentuation of agitation leading to delirium).[26]

[25] *See* Jiska Cohen-Mansfield & Nathan Billig, *Agitated Behaviors in the Elderly: I.A. Conceptual Review*, 34 J. Am. Geriatrics Soc'y 711 (1986).

[26] *See* Cohen G.D., *Biopsychiatry in Alzheimer's disease*, Annu Rev Gerontol Geriatr. (1989); 9: 216-231.

7. THE DELIRIUM

Delirium has a high probability of occurring in the demented. It must therefore be recognized and distinguished from other B.P.S.D.s. There are key criteria.
In order to speak of delirium, the following elements must be present: I) acute onset and fluctuating course; II)lack of attention.
To these must be added one of the following symptoms: III) disorganized thinking: hallucinations with agitation; IV) altered level of consciousness.

Delirium must be immediately identified. It is important to notice that it has many causes, including some "exogenous", or from external factors, and not only from dementia. Among the "exogenous" causes infections, especially urinary ones, the intake of some drugs (we remember the antibiotics of the quinolone family), malnutrition or dehydration, some metabolic diseases (liver or kidney), and changes in the caregiver or environmental surgical interventions are considered highly relevant. Some of these causes can cause delirium in a patient who is not demented, a situation that must be kept in mind in the criminal sphere, given that, in these situations, the delusion then disappears leaving a person intact. If accused of a crime during the state of delirium, it must be investigated, studied and identified.

8. ETIOLOGY OF B.P.S.D.

B.P.S.D.s arise from various causes. At the moment it is considered a single model that provides genetic alterations: receptor polymorphism, neurobiological aspects, neurochemical and neuropathological psychological aspects: personality, stress response and social aspects: changes in the environment, caregiver problems.

They depend on an alteration at the level of neuronal transmission within the central nervous system. The neurotransmitters involved in dementia are acetylcholine (the main neurotransmitter involved), dopamine, norepinephrine, serotonin and glutamate. The latter is an excitatory amino acid which, in dementia, can cause the so-called "glutamate excitotoxicity".

It must be kept in balance because its deficiency, in the long run, generates problems, including psychotic symptoms. On the other hand, with respect to the other neurotransmitters, the cholinergic deficit causes memory loss, hallucination and delirium, a deficit of dopamine causes alteration of working memory and aggression, the noradrenergic one generates depression, while the reduction of serotonin creates depression, anxiety, agitation, restlessness, aggression. Not all symptoms and signs respond to drug therapy. Some of them (anxiety, depression, sleep disturbances, mania, delusions and hallucinations, verbal or physical aggression, inappropriate sexual

behavior) can be treated to a certain extent. Others, do not respond to drugs: wandering, urinating or defecating inappropriately, dressing and undressing inappropriately, endlessly repeating acts (perseveration) or vocalizations, hoarding, eating "inedible" things, aiming or snatching the means protection, pushing the wheelchair against others or against the wall and other antisocial gestures.

9. EVALUATION OF BEHAVIORAL DISORDERS

The assessment of behavioral disturbances in patients with dementia presents a methodological and clinical challenge. The coexistence of cognitive impairment with behavioral alterations makes it difficult for both the family members and the operators to observe and characterize individual disorders. For this reason, various tools have been developed for evaluating the global and specific characteristics of behavioral symptoms.[27] Many of these assess a narrow range of behavioral disorders, without analyzing their characteristics as a whole. Direct observation of behavioral disorders is often limited to institutionalized subjects or may only be possible in specialized centers, so in most cases an interview is made with the caregiver who reports the disorders observed by him at home. There is a tendency on the part of family members to over or underestimate the present disorders, depending on the relationship with the patient or the stress due to the care burden.

Cummings developed a behavioral disorder rating scale called NeuroPsychiatric Inventory [hereinafter N.P.I.], able to assess, on the basis of information obtained from the caregiver, the frequency and severity of behavioral disorders through the use of a questionnaire.[28]

The N.P.I. allows to evaluate a wide range of behavioral disorders, for the accuracy of twelve: delusions, hallucinations, agitation-aggression, dysphoria-depression,ansia, euphoria-exaltation, apathy-indifference, disinhibition, irritability-lability, aberrant motor behavior, sleep disorders, appetite and eating disorders. The single items are explored with further sub-items that allow to obtain more detailed information. Behavioral disorders are graded with a differentiated score by frequency (0: never, 1: rarely, 2: sometimes, 3: frequently, 4: almost constantly) and severity (1: mild, 2: moderate, 3: severe). The overall score, therefore, ranges from zero to 144, and is an index of the severity of the disturbance. The evaluation of stress on the caregiver also follows, with a score from zero (none) to five (severe) for each disorder, so

[27] *See* Alberto Costa et al., *The Need for Harmonisation and Innovation of Neuropsychological Assessment in Neurodegenerative Dementias in Europe: Consensus Document of the Joint Program for Neurodegenerative Diseases Working Group*, 9 Alzheimer's Rsch. & Therapy, Apr. 17, 2017, at 1.

[28] *See* Jeffrey L. Cummings et al., *The Neuropsychiatric Inventory: Comprehensive Assessment of Psychopathology in Dementia*, 44 Neurology 2308 (1994).

the overall stress, on the twelve items, varies from zero to sixty. This scale has proved to be an objective and effective tool for the assessment of behavioral disorders in patients suffering from various types of dementia (A.D., V.D. and frontotemporal dementia); it can also be an aid in the differentiation of the various forms of dementia.[29] There are different versions of the N.P.I. for use in institutionalized patients and for self-assessment by patient caregivers.

An aspect that deserves particular attention concerns the evaluation of depression. There are numerous tools in this regard, both scales that detect the presence of depressive symptoms through direct request to patients (such as the Geriatric Depression Scale) and observational scales (better applicable even in the most serious patients). The Cornell Scale was specially designed for the assessment of depressive symptoms in demented patients.[30] It uses a standardized series of items detected through an interview with a person who knows the patient (family member or operator) and a semi-structured interview with the patient.

10. THE TREATMENT OF B.P.S.D.. NOTES ON CURRENT EUROPEAN RESEARCH.

The treatment of N.P.S. represents one of the main outcomes in the care of the demented patient and is often a challenge that requires a multimodal approach, which includes the education of family members and caregivers, the use of drugs and behavioral or other non-pharmacological procedures. The intensity of the treatment, the choice of strategies (non-pharmacological, environmental, pharmacological approach) and the choice of the type of pharmacological treatment depend on various clinical and socio-environmental factors.[31]The approach to the patient with N.P.S. requires a systematic assessment of the environmental and relational factors that may have contributed to the onset of symptoms.

An operative method is described by Kales and is called "D.I.C.E." (Describe, Investigate, Create, Examine).The program details the conditions of the patient, caregivers and the environment at each step of the approach and describes the "concrete" and environmental behavioral interventions that should be considered. In short, the components are: *D*: Describe - the situations and contexts related to the appearance of behaviors; *I*: Investigate - examine aspects of the patient's health, drug treatments, sleep disorders or physiological variables; *C*: Create - develop a plan for the prevention and management of behavioral problems shared with the caregiver and

[29] *See* Giuliano Binetti et al., *Behavioral Disorders in Alzheimer Disease: A Transcultural Perspective,* 55 Arch. Neurol. 539 (1998).
[30] *See* George S. Alexopoulos et al., *Cornell Scale for Depression in Dementia*, 23 Biological Psychiatry 271 (1988).
[31] *See* Angelo Bianchetti et al., *Pharmacological Treatment of Alzheimer's Disease*, 18 Aging Clinical Experimental Rsch. 158 (2006).

operators; *E*: Examine - evaluate the effects of the interventions and make changes if necessary.[32]

Pharmacological interventions should be reserved for situations in which N.P.S. put the patient or caregivers at risk, when symptoms are very disturbing or when non-pharmacological approaches are not possible or have been found to be ineffective.

Pharmacological treatment of B.P.S.D.s should be undertaken after making sure that B.P.S.D. have no physical causes are not caused by other drugs they do not respond to non-pharmacological interventions.

In the following cases, it is possible to make use of drugs: I)if someone has made an accurate diagnosis of the level of deterioration; II) if all non-pharmacological welfare and management measures have been applied at the family and environmental level; III)if the cause of the symptoms, for example a disease, has been looked for; if the possible side effects of the drugs have been evaluated according to the characteristics of the patient; IV) if the particular response to drugs of the demented subject has been considered, for example the paradoxical effect of benzodiazepines.

A European multicentre study is underway, funded by the European Union, of which the undersigned is part as coordinator of the Dementia Center of the Mantua Hospital.[33] The study is called RECage (REspectful Caring for the AGitated Elderly), and it is committed to identifying the most effective ways of taking charge and treating behavioral decompensation, which often requires temporary hospitalization of the patient in the so-called Special Care Unit type B [hereinafter S.C.U.-B.] centers where an attempt is made to treat the disorder with non-pharmacological treatment, allocating this only to temporary phases. The results are compared with those obtained by the Special Care Unit type A [hereinafter S.C.U.-A.], where the patient is received and treated pharmacologically. The leaders of this study are Prof. Carlo Alberto Defanti and Dr. Sara Fascendini, respectively Health Director and Primary of one of the S.C.U.-B. leaders in Italy, the one present in Gazzaniga (B.G.), managed by F.E.R.B. Onlus. This is due to the fact that, to date, there are no univocal answers on the strategies to be adopted in the event of behavioral decompensation. There are ten European hospitals enrolled, including the Dementia Neurology Center of the Civil Hospital of Mantua, coordinated by the author.

In S.C.U.-A., where behavioral decompensation is treated pharmacologically, there are rules for prescribing the therapy:I)In the demented elderly the dosages are

[32] *See* Helen C. Kales et al., *Management of Neuropsychiatric Symptoms of Dementia in Clinical Settings: Recommendations from a Multidisciplinary Expert Panel,* 62 J. Am. Geriatric Soc'y 762 (2014).

[33] *See* Mirko Avesani et al., *Respectful Caring for the AGitated Elderly*, Asst Mantova (https://www.asst-mantova.it/recage) (last visited Feb. 12, 2022).

lower than in the young and non-demented people; II) Hypoalbuminemia causes the drug to remain in the site of action for longer; III) Reduced hepatic and renal metabolism slows their elimination with the risk of toxicity and interaction; IV) Their half-life is increased because being lipophilic they accumulate in the increased fat mass of the old man. V)Lewy's dementia manifests hypersensitivity to neuroleptic drugs.

The drugs to be prescribed belong to the families of antipsychotics (typical and atypical, i.e. first and second generation), of antidepressants, benzodiazepines, and anticonvulsants. Obviously, the pharmacological choice cannot be separated from a correct nosographic and nosographic identificationetiopathogenesis of the B.P.S.D. type.

11. INVESTIGATORS RECOMMENDED IN INVESTIGATED / ACCUSED PATIENTS

By now, the classic psychiatric report is completely outdated, considering that, as we have seen, there are neuropsychiatric symptoms associated with dementia, which are of neurological relevance.

First of all, a thorough neurological evaluation is needed with at least first and second level tests (by first level the author suggests e.g. the Mini Mental Test Evaluation, [hereinafter M.M.S.E.]; by second level the author suggests e.g. the clock test and the Frontal Assessment Battery [hereinafter F.A.B.]. The integration of the clinical examination (which highlights any apraxias, or visual field deficit, or language deficit in informal interview, or orientation deficit or presence of delusions and hallucinations, as well as neuromotor focal deficits) with these three tests, allows the diagnoser to investigate different cognitive functions, both cortical and subcortical, both frontal, temporal lobe and hippocampus.

To these tests, the N.P.I. scale must be applied, to better investigate behavioral disorders and the Geriatric Depression scale [hereinafter G.D.S.], a scale that helps us to understand the degree of depression and the quality of the head in the context of a possible decay. cognitive with probable dementia manifestation.

It is also important to understand the progress and time of presentation, if it was gradual and progressive or acute / subacute. It is essential to understand if the disorders are fluctuating or persistent, if they reduce the person's personal autonomy. Below we present the two rating scales Activities of Daily Living [hereinafter A.D.L.] and Instrumental Activities of Daily Living [hereinafter I.A.D.L.].

To calculate the A.D.L. index, a simplified scale is used which provides for the assignment of a point for each independent function in order to obtain a total

performance result ranging from 0 (complete dependence) to 6 (independence in all functions). For the attribution of the score it is necessary to translate the three-point assessment scale (without assistance, partial assistance, or complete assistance) into the dichotomous classification "employee / independent". Also for the calculation of the I.A.D.L. index, a simplified scale is used which provides for the assignment of a point for each independent function in order to obtain a total performance result that varies from 0 (complete dependence) to 8 (independence in all functions). After this evaluation, it is advisable to proceed with the complete Neuropsychological tests, in order to have both a confirmation and a better characterization of the deficits.

It is acceptable, if the patient is being investigated for a differential psychiatric pathology diagnosis, to proceed with the personality tests: Minnesota Multiphasic Personality Inventory-2 (M.M.P.I.-2); Million Clinical Multiaxis Inventory-III (M.C.M.I.-III); Dissociative Experiences Scale-III (D.E.S. II). In subsequent steps, we move on to laboratory and instrumental evaluation, which have now become fundamental. At the laboratory level, by means of a lumbar puncture we evaluate the alterations of some cerebrospinal fluid (C.S.F.) proteins (protein 14.33, sign of neuronal necrosis; protein TAU, pTAU, B-amyloid 1-42, ratio pTAU / B-amyloid 1-42) and the presence of some antibodies that today characterize some forms of encephalopathy, autoimmune encephalopathies (among these antibodies to N-methyl-D-aspartate (N.M.D.A) receptor, and other neuronal receptors). They are newly discovered encephalopathies that can begin with neuropsychiatric disorders as well as with epileptic seizures. The onset of a disorder of this type, in a person who was in full well-being, must always make us keep this possibility in mind. At the instrumental level, in addition to a classic M.R.I., a morpho volumetric M.R.I. is essential to understand which brain areas are subject to atrophy. It is also important to perform a P.E.T-C.T. scan with fludeoxyglucose, to highlight brain areas with.. reduced cerebral metabolism, to be compared with neuropsychological tests and clinical examination. Furthermore, a new method is gaining ground: Functional Magnetic Resonance Imaging [hereinafter f.M.R.I] in resting state mode. This method, combining the high temporal definition of the electroencephalography [hereinafter E.E.G.] (in the order of multiple sclerosis) with the high definition of the f.M.R.I, allows to highlight activations and deactivations related to brain electrical biorhythms using the so-called independent components (I.C.A.) technique.