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Behaviour disorders dopamine-related

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Introduction

In recent years the literature on disorders of cognitive functions in Parkinson's disease has reached a wide importance and size. The attempt to contextualise and interpret psychological disorders that characterize Parkinson's disease are already in the 19th century: James Parkinson in his An Essay on the Shaking Palsy "in 1817, while denied the existence of disorders of the senses and the intellect, described patients as" unhappy, discouraged and melancholic. Charcot already asserted that often psychic faculties were compromised and believed that the emotional tension played an important role in the pathogenesis of the disease. Regis for first parkinsoniani classified as mental disorders that characterize them: a first level of gravity they would encounter a simple changes of mood and personality of depressive type, to a second level more serious show hypersensitivity, irritability and egocentrism to the highest levels of severity characterized by hallucinations and a great weakness with global capabilities and mental decay.
These observations were made in the era-DOPA, then completely independently from influences induced by this drug (as well as by dopaminergic agonists and anticholinergics) intellectual functions and emotions.

Today there is a growing awareness that in Parkinson's disease can occur motor disorders and, among the latter is typical dependencies relating to the substance, commonly known as the dopamine dysregulation syndrome or DDS characterized by the use of dopaminergic drugs in doses higher than those required to treat motor symptoms despite the development of disabling dyskinesias, which behavioral dependence syndromesusually framed in the context of impulse control disorders which include ICDs, or hypersexuality, compulsive shopping, compulsive gambling etc (1-4).
The latter is the only one to have won the inclusion in the DSM, under the category of impulse control disorders not Elsewhere classified, becoming, for the scientific community, a psychiatric disorder itself. The impulse control disorders referenced are those not classified as part of clinical disorders in other sections of the DSM IV (e.g., eating disorders, Substance-related Disorder paraphilias, Antisocial personality disorder, schizophrenia, mood disorders can have events involving problems of impulse control). The fundamental characteristic of impulse control disorders is the inability to resist an impulse for a compelling desire, or the temptation to make a dangerous action for themselves or for others in the majority of disorders described in this section, the subject is a growing feeling of tension or excitement

before the action, and then try pleasure, gratification, or relief when committing the action itself. After the action may be more or less remorse or guilt. The phenomenon of impulsiveness combine several subfactors: generic tendency to action, inability to delay gratification, inefficiency of inhibitory factors (concern for consequences and reduced ability to mentalise) (5).

In this section include the following disorders:

Intermittent Explosive disorder, which is characterized by occasional episodes of inability to resist aggressive impulses, which cause serious damage or destruction of property.

Kleptomania, that is characterized by recurrent failure to resist the urge to steal objects that have no commercial value or utility.

Pyromania, which is characterized by habit to set fire to pleasure, gratification, or relief of tension.

Pathological gambling, which is characterized by many difficulties in limiting money and/or time spent on gambling which leads to adverse consequences for the gambler, others, or for the community..

Trichotillomania**,** which is characterized by compulsive urge to pull out one's own hair leading to noticeable hair loss, distress, and social or functional impairment

Impulse control disorder not otherwise Specified.

In subjects with pathological gambling may be distortions of thought (e.g. negation, superstition, excessive self-confidence, a sense of power and control). Diagnostic criteria:

a) persistent and recurring gambling behavior, as indicated by at least 5 of the following points:

-Is excessively absorbed by gambling (e.g. think of when you play, how to get the necessary money …);

-Needs to gamble with increasing amounts of money to achieve the desired excitement;

-Has repeatedly attempted to control or stop the game;

-Is restless and irritable when trying to resist the game;

-Play gambling to escape problems or of relieving a dysphoric disorder mood (anxiety, guilt, depression, etc.);

-Tendency to continue playing for chasing their losses;

Mind-the other for concealing the extent of the problem;

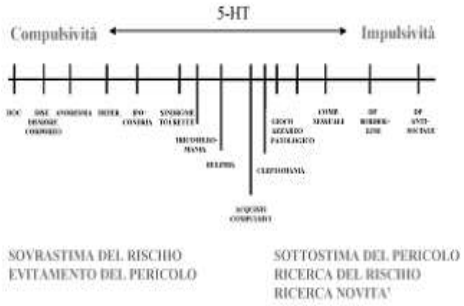
-Has committed illegal acts to finance gambling;

-Put in jeopardy or lost a significant relationship, job or a career opportunity for gambling;

-Relies on others to find the money to relieve a desperate financial situation caused by gambling.

(b)) The gambling behavior is not better accounted for a manic episode (6).

DCI may be included in a single family of compulsive-impulsive disturbances of spectrum, a dimensional continuum which sees on one extreme the DCI incurred by pleasure and activation, and compulsive disorders guided by the need to reduce anxiety (7).



So rather than see them dimensionally opposed to obsessive-compulsive disorder, impulse control disorders can be represented as a phenomenologically different of a group of disorders with a common decreased ability to inhibit motor response due to certain affective States.

Nerve structures involved in impulsivity

Current knowledge highlight the role of the prefrontal cortex and its modulation on hypothalamic activity and limbic and dysregulation of different neurotransmitter systems, such as serotonin, noradrenergic, dopaminergic, GABAergic with additional evidence to system load and opiate of the androgenic hormones. Impulsiveness, considered today a biologically determined model for behavioral, behaviors implemented quickly, with little planning and poor assessment of the consequences of their actions. Characteristics of impulsive behaviors are difficult to use the information available to assess the possible consequences of their actions, the difficulty to defer instant gratification in favor of a larger but more distant, fix temporally to inhibit motor responses. Today, the analysis of impulsiveness is possible at several levels: genetic, neural, cognitive and behavioral.

Genetic analysis shows that certain polymorphisms (such as protein DAT) affect the levels of impulsivity (8-9). The structural and functional neuroimaging techniques identify a dysfunction of the prefrontal cortex as likely neurobiological substrate of a high level of impulsivity (10-11).

According to the psychometric approach impulsiveness is ' specific traits of temperament as "Novelty Seeking" which is believed to depend on high levels of dopaminergic stimulation: these players are easy to the enthusiasm and to explore, get bored easily, are prone to impulsivity, unstable rationally and fickle decisions (12)
Neuropsychological approach describes the impulsivity as a result of underlying processes neurocognitive and therefore measurable through specific parameters (13). Impulsiveness can be considered as the result of a lack of inhibitory control is a deficit of integration capacity contingency reinforcement/punishment for their actions (14).
Deficiency of two cognitive processes can lead to different forms of impulsiveness.
A first trial concerns the ability of self-control, i.e. the ability to inhibit Behavioral responses. Inhibition of response is assessed through the tasks of GoNoGo and Stop at the signal; inhibition of the response is an executive function lower prefrontal cortex dependent or VL (15).

The second aspect of impulsiveness in their ability to integrate the contingencies of reward/punishment in the choice of two or more options. In decision-making task impulsiveness is associated with a reduced ability to tailor their choices changes reinforcement contingencies/punishment. The evaluation of these and their integration in decision-making is based on the functioning of the cortex orbitofrontal and its connections with Subcortical structures of the limbic lobe as the amygdala, the nucleus accumbens and ventral striatum cortex OF, thanks to these connections, allows automatic processing and emotional stimulus with the characteristics of reinforcement/punishment, i.e. their emotional valence organizing any physiological responses (16).

Neurobiological basis of impulsivity are not yet fully understood. (fare bibliog)

Jobs at the base of addiction are, in fact, substances or behaviors that have activity of positive reinforcement, with consequent transition from learning processes reward-based to a habitual action/compulsive (17). Conditional desire, defined as the process through which a new reward is learned and acquired his connoted motivational, is an element of undisputed importance (18).

The neuro-anatomical structures involved in the conditioning process include the amygdala, deputy to the assignment of emotional connotations, orbito-frontal cortex, which encoding the outcome of the behavior and the anterior cingulate cortex implicated in learning and cognitive control discriminating power. Other potentially involved are represented by the hippocampus involved in mnesic in stimulus report and motivational, hypothalamus and nuclei partitions, which provide information for the motivational behaviors (19-20).

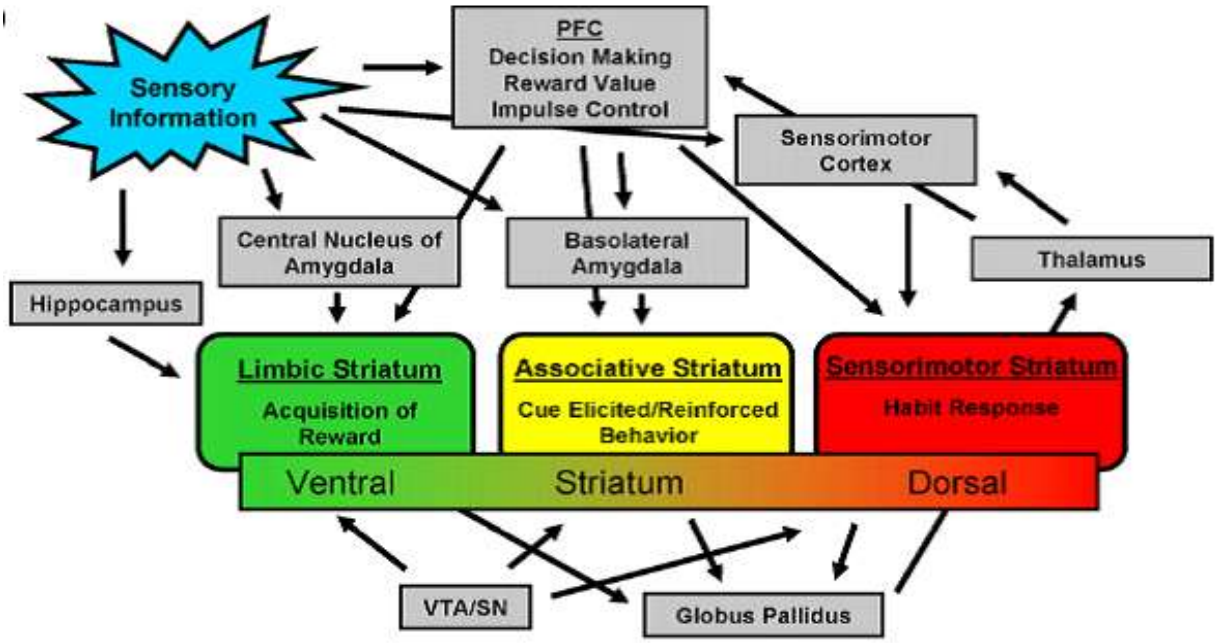
Another structure involved in the preparation and the addiction is represented by the Nucleus Accumbens, which is composed of one schell and a core. The shell has a reciprocal innervation with ventral tegmental area, playing a role in the modulation of the motivational significance, while the core seems to be involved in the expression of learned behaviour in response to stimuli that predict the reinforcement (21).

The ventral tegmental area concentrate its facilitation role through a phase of dopamine release in the direct projections to the nucleus accumbens, amygdala and prefrontal cortex (including orbito frontal cortex and anterior Cingulate gyrus) during events with emotional connotations. The dopaminergic neurons are inhibited, probably through the medial dorsal thalamus, when not to the reward (22)

It was also suggested a influence on subsequent behavioural impulses in the stadiums, corticostriatali circuit involved when the action level becomes compulsive (23).

It follows a pattern in which a stimulus can generate "desire" involves the activation of the shell of the nucleus accumbens using input from the temporal (hippocampus), ventral tegmental area and from the prefrontal cortex;

"transit" to a conditioned reinforcement at the core of nucleus accumbens through input from the amygdala and prefrontal cortex, and finally evolves in structuring the dorsal striatum habit from the bark sensor-motor. This transition would involve limbic areas therefore, associative and sensorimotorie regions of striatum (24-25).



The prefrontal cortex modulates ipotalamiche and activities: limbic lesions of the dorsal prefrontal cortex are associated with deterioration of the ability of long-term planning and increased apathy, while the orbital portion lesions are associated with increased emotional responses reflected to environmental stimuli (26-27). Lee and Coccaro, with studies of Positron Emission Tomography (PET) have documented a decreased serotonin function in specific brain regions, including the prefrontal cortex in subjects with increased aggression and impulsiveness.

Other areas involved in impulsivity and aggressiveness are the medial thalamus, preoptic, mammillary bodies, the hippocampus and the basal ganglia (28-29).

Anomalies of the frontal lobes are associated with inability to delay or inhibit certain impulsive actions, and inability to calculate the probability of risk negative or the outcome of a given behavior. Impulsiveness is part of the basic manifestations of frontal lobe syndromes: patients with damage to the hypothalamus part of the frontal lobes are not responsive to stimuli emotionally, indicating that the frontal cortex is involved in the decision-making process(30). Bechara et al., studying the pathological gambling, have suggested that players with injury to the frontal cortex in the hypothalamus are unresponsive to future consequences, both positive and negative, and are solely driven by immediate benefits. Patients with hypothalamus injury making choices to prefontale bilateral test "gambling task" which give immediate rewards though encumbered by high losses in the long term (31). This limit in decision-making capacity is similar to that of subjects that abuse of cocaine, opiates or alcohol (32). Other confirmations on the role of the frontal lobes in impulsivity are studies on cerebral metabolism in patients with impulsive and aggressive (33) and cerebral flow of pathological gamblers (34).

The hypothalamus is involved at various levels, such as the sleep-wake cycle, body temperature, appetite and sexual activity. Together with the pituitary gland is the largest regulator of autonomic nervous system. All streets, mesolimbic and ascending dopaminergic serotonin, noradrenergic and cholinergic brainstem have endings hypothalamic level. The hypothalamus plays a key role in the expression of aggression in animals (35). Hypothalamic lesions in humans seem to be associated with aggressive behaviors and unplanned unfinalized often turn out to be caused directly but generated by a State of physical discomfort (36-37-38-39).

The amygdala Activation media and/or inhibition of the hypothalamus and modulates the input from the cortex. As other limbic structures, induce emotional behavioural responses in relation to environmental events on the basis of past experience. The amygdala, given the central role in the limbic system, is considered a fundamental structure for mediation, perception and expression of emotions such as fear and anxiety, which couples the sensory experiences (direct to the hypothalamus) with affective state or certain behaviors such as anger, playing a monitoring role, balancing and modulation. Lesions at the level of the amygdala induce a reduction of emotional response (40-41).

The thalamus gathers sensory stimuli coming from external receptors (eyes, ears, skin), makes a first processing, then send the results to specialized areas of the brain which, in turn, send information to the amygdala to organize the response of the organism to external event.

However, if you need a quick response of the organism (e.g. fight-flight), the thalamus sends the results of its processing directly to the amygdala, without going through the rational mind of the cortex.

The amygdala is the part of the limbic system specializing in emotional matters. It operates as an archive of emotional memory and is, therefore, custodian of the meaning of events. In fact, if is removed, the result is the inability to assess the significance of emotional events.

Incoming signals from the sensory organs allow the amygdala to analyze every experience, making it a sort of "watchdog" who scours every emotion and every perception, guided by questions that have roots in the mists of time: "it's something I'm afraid, is something that I hate, it is something that hurts me, is something that I want?"

If the answer is affirmative, the amygdala reacts immediately by sending a warning message to all parts of the brain. In this way, it stimulates the secretion of hormones that trigger the reaction of fight, flight or pleasure, and activates the muscular and cardiovascular system.

This reaction of the organism can be however organized according two different paths.

The direct route thalamus-amygdala involves a quick, but inaccurate, that allows you to respond to potentially dangerous stimuli, before you know exactly what they are.

The thalamus-precortex-amygdala, instead, an emotional response mediated by rationality because details are encoded stimuli from the thalamus, to create a detailed and accurate representation that allows for an assessment and a more emotional response compared to the weighted path thalamus-amygdala.

So, if the immediate intervention of the amygdala is useful in dangerous situations, precorteccia's intervention prevents the amygdala to unleash harmful emotions such as anger or disproportionate aggression (40-41)).

Various neurotransmitter systems have modulation action on impulse control disorders.

Have been observed evidence of a dysregulation of serotonin and presinaptico deficit of serotonin available, regarding a wide variety of impulse control disorders: research on men and animal models show the role of serotonin (5-HT) centrally in the inhibition of impulsive behaviors and its dysregulation in dysfunction or disorder characterized by impulsiveness and aggressiveness (42-43-44).

Some studies have shown the presence of higher levels of serotonin in animals that had a dominant and aggressive(45-46) behavior. Mice mutant which lacks the 5-HT1B receptor are compared to the sample population, more impulsive, aggressive behaviour and a greater tendency to dependence on substances such as cocaine and alcohol (47-48)

The opioid system seems to be involved in the Neurobiology of aggression. The observation that the naloxone and naltrexone improve self-damaging behaviour suggests that an alteration of the opioid system is involved in the pathophysiology of these carried out aggressive (49). Animal models it was found that the up-regulation of the μ opioid receptors for limbic areas is correlated with an increase in emotional and aggressive behaviors the dopamine is not only involved in the movement control volunteers, but also plays a significant role in the reward system of the brain and in the modulation of behaviors. Therefore, most if not all PD patients, will be susceptible to this type of pathology (50).

Dopaminergic activity, especially at the level of mesocorticolimbic, is of central importance in the mediation of gratification and reinforcing behaviors and even opioid μ receptors are involved in these mechanisms (51-52-53).

The possible role of the aggression is suggested by the fact that the blocking of D1 and D2 receptors for by produces effects that antiaggressiv disabilities (54). It was pointed out that when there is a malfunction in the mechanisms of gratification--that could be due to an alteration of the genetic type of the dopaminergic system-presumably we are facing a condition characterized by traits hypodopaminergic that favors in affected, search behavior, substance abuse and substance dependence to overcome this deficiency. Substances such as alcohol, cocaine, heroin, marijuana, nicotine, glucose, stimulate a neuronal activation and a release FROM that can satisfy the yearning.

The lack of D2 receptors determines a high risk of propensity toward multiple behaviour characterized by dependency, impulsivity and compulsivity ranging from substance dependence and abuse, binge eating sugar, pathological gambling, ADHD, Tourette Syndrome, autism, chronic violence, conduct disorders, antisocial behaviour and sexual addictions (55-56).

Other neurotransmitter systems as well as serotonin, GABA and NA, although the latter with some controversy, seems to affect certain behaviors of type impulsive and aggressive (57). Some studies have identified that for example the levels of GABA in the central nervous system of male mice are directly related to the aggression, while receptive to benzodiazepines sensitivity is inversely proportional to aggressive behaviors (58).

The role of GABA is also shown indirectly through effects that have small amount of alcohol in the aggression through positive modulation of receptor complex (59).

Neurobiology of ICD in patients whit Parkinson's disease

The pathophysiology of ICD therefore affects neurotransmission systems specific regions of the brain and neuronal circuits.

Until today only few studies with functional imaging were used to test in vivo the pathophysiology of the ICD in patients with Parkinson's disease.

In 2005 Reuter and colleagues published the results of a study conducted on 12 pathological glambers (PG) suffering from Parkinson's disease and 12 control patients, using functional MRI and a card game known to exert a strong ventral striatal activation study showed that, during the simulation game, patients with PG, if compared to control caseshave a diminished activation of the prefrontal cortex and hypothalamus, ventral striatal areas involved in the processes of reward. The authors therefore suggested that there could be some sort of ipofunzione of basal ganglia in patients with PG, and that such pathological behaviour would be implemented to compensate for the deficiency of activation; the physiopathological model proposed would therefore close similarities with substance dependence (60).

In 2006 Evans and colleagues conducted a study on a small group of PD patients with and without DDS, using methodical raclopride PET, a specific ligand D2. Have not been observed substantial differences in the percentage of reduction of radiotracciante between patients with and without DDS after administration of l-dopa in the dorsal striatum while the ventral striatum has highlighted a significant decrease of raclopide tied after l-dopa exclusively in patients with DDS, indicative of a good functional reserve in that system.

The data suggests that the compulsive use of dopamine replacement therapy used by the PD with DDS could be traced back to a ventral circuit awareness striatal (61).

Similar results, using different methods, have been obtained in a recent study of Cilia. 11 patients with PD and PG were evaluated by SPECT perfusional analysis of the data showed an increase at rest in the basal ganglia, orbit-frontal cortex in the hippocampus, the amygdala and insula compared to patients without PG affeti by MP; indicative of a specific functional abnormality in the mesocorticolimbic network. The authors concluded that in patients with PG there is a relative integrity of mesocorticolimbic, concurrently with the pathological changes of dorsal striatale of Niger. Then PG could develop following an abnormal stimulation drug induced in patients with Parkinson's disease in which the circuit mesocorticolimbic remains relatively little compromise (62).

Recently Steeves et al. have published data about the release of dopamine striatale investigated by PET in patients with PD and PG while executing task simulants a gambling. In PD patients with PG has observed a major decrease of radiotracer ventral striatum during the "gambling", indicative of an increased dopaminergic release (63-64)..

It was also noted that the rapid decrease of the title of the ligand in patients with PD PG was observable during the execution of a task. The authors have interpreted the data as an index of a low density D2/D3 receptor (65-66-67).

Studies employing the ERPs, the subjects are evaluated from the standpoint of neuropsychological and clinical, and analyzed such correlations with electrophysiological parameter indexes of cognitive, motor and involvement with the kind of treatment.

The event-related evoked potentials have been widely used in the study of Parkinson's disease. The most studied was the P300, particularly its latency, which correlates to the degree of cognitive impairment.

From an in-depth analysis of the literature showed that patients not bedridden, suffering from the disease, showed an increase in latency of P300, obtained by the classical paradigm auditory "oddball", compared to normal subjects of equal age (68)

Other authors agree in stressing an increased latency, even if no such entity to reach statistical significance (69).

In addition, drug therapy may interfere with potential lenses.

Studies that have compared patients de-novo with patients in the course of drug therapy domaminergic therapy that seems to induce a reduction in P300 latency. The latter indeed compared with that of the control group, does not differ significantly after treatment (70 -71).

Other authors, though not always in agreement with other studies reporting data in favour of an increase in latency of P300 demented patients in old age, or belonging to a more severe stage of the disease (72).

A direct correlation but not significant was detected between the P300 latency and age of the patients. In addition, the increase in latency with age is more pronounced in patients with Parkinson's disease compared to controls.

The same Author not found correlations between P300 latency and clinical severity of disease, measured with the scale of Hoehn and Yahr. This would take the P300 a decisive separately explore the involvement of cognitive function than motor.

Furthermore, by analyzing the correlations between P300 and clinical data, was found a highly significant inverse correlation between the P300 latency and the degree of cognitive involvement, expressed by scores of the Mini-Mental State Examination: an increase in latency was reduced scores themselves and thus a higher degree of cognitive impairment (73). The data on the magnitude of the P300, in patients with Parkinson's disease, although more inconsistent, seem to detect an overall reduction of that parameter (74). The same subjects seem to present abnormalities in components N1, P2 and N2. The data, not always statistically significant, agree with an increase in latency and a decrease in the amplitude of the above components.

Studies that have used for the detection of ERPs paradigm "oddball" with Visual stimulation or a type of Multimode paradigm (Visual/acoustic) bring data equivalent to those previously described, and then confirm the same electrophysiological abnormalities in Parkinson's disease. All these figures can be considered the expression of a "slowdown" generalized affecting cognitive activity-related functions, in addition to the purely physical, involved in the processes of selective attention required from the paradigm of stimulation from the test run (75).

Objectives of the study

Cognitive and behavioral abnormalities are frequent in Parkinson disease (PD), but their related anatomical are still uncertain. Several studies of functional magnetic resonance imaging, neuropsychological and neurophysiological assessment tests are carried out to verify any factors predictive of disease and to better identify possible relationships between biological damage and phenomenological expression of the same damage.

Impulse control disorders in patients suffering from Parkinson's disease would be to frame as processes psychopathological persons disinhibitors, induced by an aberrant dopaminergic stimulation, developed from a population of patients.

The more brain areas involved include the prefrontal cortex, the majority of areas ventromediali and orbitofrontali, the ventral striatum, nucleus accumbens and amygdala (76-77-78).

Objective of the study is to determine any changes morfostrutturali and frontal circuits potentially involved in the development and maintenance of "behaviour addiction", by neuroimaging and neurophysiological methods in patients with Parkinson's disease with impulses control disorder.

Materials and methods

In the study of 8 patients with Parkinson's disease with at least an impulse control disorder, particularly 8 pathological gambler (ICD+), diagnosed through a structured interview in accordance with the diagnostic criteria of DSM-IV-TR. They were also enrolled a control group of 8 patients with non-demented Parkinson disease with comparable clinical and demographic characteristics who had not demonstrated behavioural abnormalities (ICD-).

Demographic characteristics of the population

	PD + ICD	PD ctrl
Age	68,0 ± 6,4	68,5 ± 7,2
L-Dopa dose equivalent*	632,6 ± 332,2	598,4 ± 284,0
UPDRS part III – on state	15,2 ± 3,2	12,2 ± 1,9
Disease duration	9,2 ± 2,2	8,9 ± 2,9
MMSE	26,6 ± 1,6	27,2 ± 1,8

*100 mg of L-dopa =130 mg of controlled-release L-dopa =70 mg of L-dopa + inibitore catechol-*O*-methyl-transferase =1 mg of pramipexolo = 5 mg ropinirolo.

All patients were subjected to sequences of DTI , neurophysiological determination of P300 and a standardized neuropsychological tests battery.

Patients were subjected to a magnetic resonance imaging with conventional sequences and DWIs in 15 space directions (diffusion tensor imaging) and T1 weighted sequences volumetric.

The analysis of diffusion tensor images was carried out with the correction of artifacts from distortion, were extracted images parenchyma as a mask and the images are then processed to create a model of diffusion tensor of every single patient.

The data of the fractional anisotropy (FA) and mean diffusivity (MD) have been riallineante on a standard model.

Individual masks were created which included both the superior and middle frontal gyrus bilaterally.

Were therefore calculated for each mask both right and left values for CAUSES and MD (65-66-67).

The **P300** (P3) wave is an event related potential (ERP) elicited by infrequent, task-relevant stimuli. It is considered to be an endogenous potential as its occurrence links not to the physical attributes of a stimulus but to a person's reaction to the stimulus. More specifically, the P300 is thought to reflect processes involved in stimulus evaluation or categorization. It is usually elicited using the oddball paradigm in which low-probability target items are inter-mixed with high-probability non-target (or "standard") items (79). When recorded by electroencephalography (EEG), it surfaces as a positive deflection in voltage with a latency (delay between stimulus and response) of roughly 300 to 600 ms. The signal is typically measured most strongly by the electrodes covering the parietal lobe. The presence, magnitude, topography and timing of this signal are often used as metrics of cognitive function in decision making processes. While the neural substrates of this ERP still remain hazy, the reproducibility of this signal makes it a common choice for psychological tests in both the clinic and laboratory (80).

Since the initial discovery of this ERP component, research has shown that the P300 is not a unitary phenomenon. Rather, we can distinguish between two subcomponents of the P300: the novelty P3, or P3a, and the classic P3, or P3b (81). The P3a, or novelty P3 (82.), is a component of time-locked (EEG) signals known as event-related potentials (ERP). The P3a is a positive-going scalp-recorded brain potential that has a maximum amplitude over frontal/central electrode sites with a peak latency falling in the range of 250-280 ms. The P3a has been associated with brain activity related to the engagement of attention (especially orienting and involuntary shifts to changes in the environment) and the processing of novelty (83). The P3b is a positive-going ERP amplitude (usually relative to a reference behind the ear or the average of two such references) peaking at around 300ms, though the peak will vary in latency from 250-500ms or later depending upon the task(84.). Amplitudes are typically highest on the scalp over parietal brain areas.(84) The P3b has been a prominent tool used to study cognitive processes, especially psychology research on information processing. Generally speaking, improbable events will elicit a P3b, and the less probable the event, the larger the P3b. However, in order to elicit a P3b, the improbable event must be related to the task at hand in some way (for example, the improbable event could be an infrequent target letter in a stream of letters, to which a subject might respond with a button press). The P3b can also be used to measure how demanding a task is on cognitive workload (85). Since the mid 1980s, one of the most discussed uses of ERPs such as the P300 is related to lie detection. In a proposed "guilty knowledge test " (86) a subject is interrogated via the oddball paradigm much as they would be in a typical lie-detector situation. This practice has recently enjoyed increased legal permissibility while conventional polygraphy has seen its use diminish, in part owing to the unconscious and uncontrollable aspects of the P300.

The P300 has a number of desirable qualities that aid in implementation of such systems. First, the waveform is consistently detectable and is elicited in response to precise stimuli. The P300 waveform can also be evoked in nearly all subjects with little variation in measurement techniques, which may help simplify interface designs and permit greater usability. The speed at which an interface is able to operate depends on how detectable the signal is despite "noise." One negative characteristic of the P300 is that the amplitude of the waveform requires averaging of multiple recordings to isolate the signal. This and other post-recording processing steps determine the overall speed of an interface (87). Scientific research often relies on measurement of the P300 to examine event related potentials, especially with regard to decision making. Because cognitive impairment is often correlated with modifications in the P300, the waveform can be used as a measure for the efficacy of various treatments on cognitive function. Some have suggested its use as a clinical marker for precisely these reasons. There is a broad range of uses for the P300 in clinical research (88).

Assessment psycophisiologico by logging Event-Related potentials or Event-Related Potentials (ERPs) in particular the family of P3. To run task patients were sitting on a comfortable chair, soundproof and in dim light, wearing a headset and holding a button. The electrophysiological signal was recorded through exploring Ag/AgCl electrodes placed at Fz, Cz, Pz, F3, F4, C3, C4, P3 and P4, according to the international system 10-20; all the electrodes had a reference bimastoideo. The Earth was represented by an electrode site on the forehead. The signal was filtered in the capture phase with a bandwidth of between 0 and 30 Hz. The eye movements (EOG, electro-oculogram light rise) have been registered with two electrodes placed one above and one below the left eye. The resistance of the electrodes has been maintained < 3 KOhm.. All subjects were genotyped 2 paradigms.

All patients were subjected to a battery of standardized neuropsychological tests evaluate the cognitive functions (MATTIS DRS), the frontal executive functions/(FAB, Wisconsin Card Sorting Test-WCST-tests verbal fluency and Semantics; Testing Courses and Verbal Span; Raven's Colored Progressive Matrices) and cognitive functions (Rey's auditory) (89). It was also performed a neuropsychiatric evaluation using NPI and GDS (90).

Results

Study results of neuroimaging

	Park + ICD (n=8) mean(SD)	Park ctrl (n=8) mean(SD)
FA SUPFRON DX	0,24(0,03)	0,22(0,03)
MD SUPFRON DX	1,14(0,28)	1,07(0,16)
FA SUPFRON SIN	0,23(0,03)	0,20(0,04)
MD SUPFRON SIN	1,11(0,27)	1,12(0,17)
FA MIDFR DX	0,23(0,04)	0,20(0,02)
MD MIDFR DX	1,06(0,23)	1,04(0,15)
FA MIDFR SIN	0,21(0,04)	0,18(0,02)
MD MIDFR SIN	1,09(0,20)	1,11(0,15)

The two groups have had no statistically significant differences evaluated using t-Student test, although patients with ICDS have shown average levels of FA tend to higher

Results of neuropsychological development

	Park + ICD	Park ctrl
MATTIS DRS	115,2 ± 8,7	121 ± 6,8
RAVLT	39,1 ± 3,5	40,2 ± 3,8
Corsi's test	3,4 ± 0,7	3,6 ± 0,6
FAB	15,6 ± 1,6	16,1 ± 1,8
Verbal Fluency –sem	13,6 ± 2,1	14,1 ± 2,2
Ravens's matrices	16,82 ± 2,23	17,26 ± 2,81
WCST	103.2 ± 13.3	92,5 ± 15,1*
GDS	9,0 ± 2,4	7,2 ± 4,1
NPI	23,0 ± 2,6	15,9 ± 2,6*

In assessing NP the only statistically significant differences have emerged the WCST and NPI.

P300

Amplitude and latencies were measured in N1, P2, P3 in N2 and giving relief to Pz paradigms for the Oddball paradigm and Fz for "novelty P3" (figures 1, 2 and 3).

M. Parkinson's patients + ICD

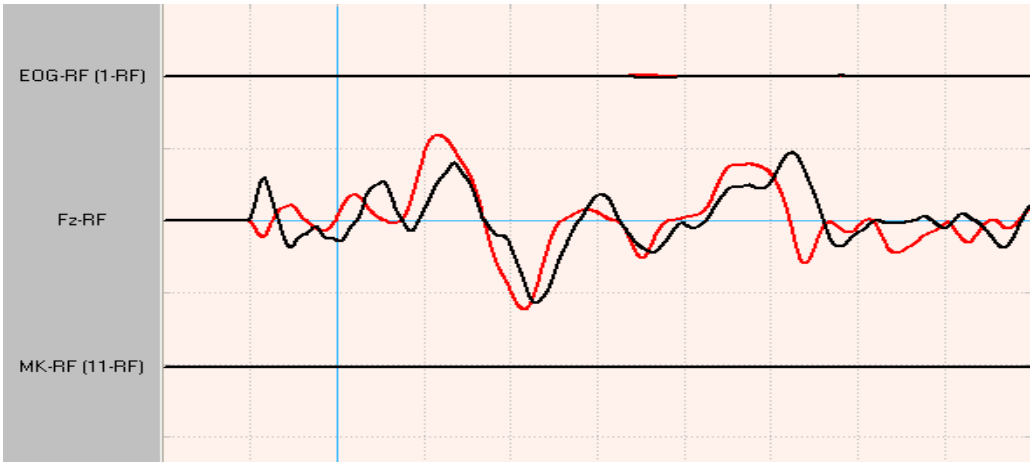
In the novel paradigm p3a was recognizable in all subjects. Its average latency was 370.31 ± 33.17.

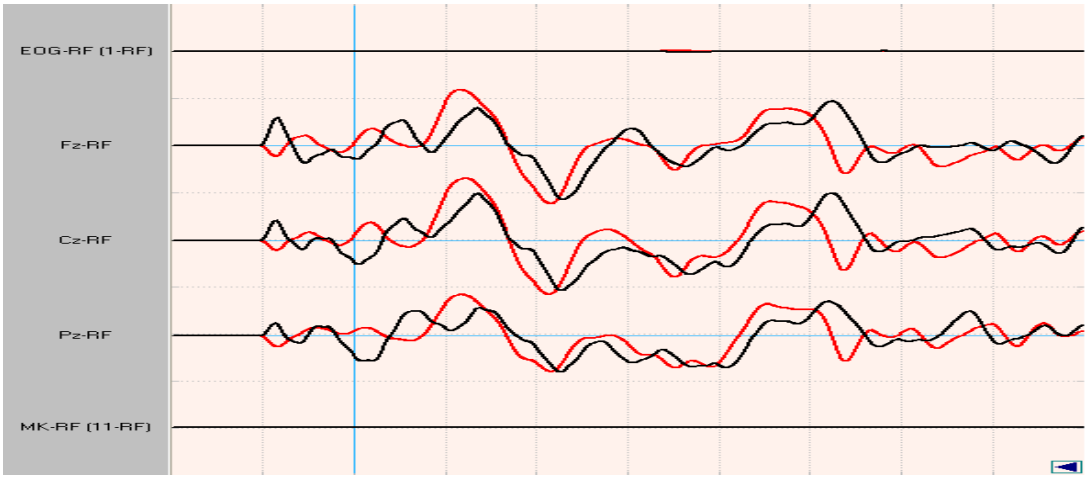
The p3b elicited with the oddball paradigm was recognizable in all subjects, and had an average latency of 382.25 ± 48.37. The average response time was 382.7 ± 65.49.

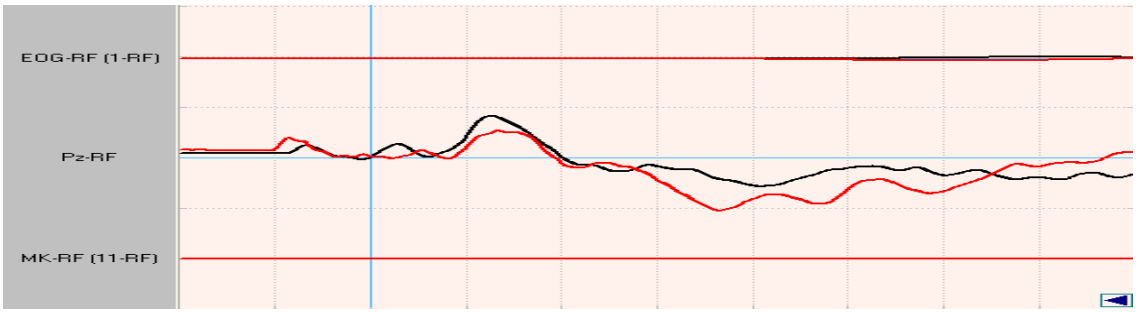
M. Parkinson's patients

The p3a was recognizable in all subjects. Its average latency was 389.64 ± 41.61.

The p3b elicited with the oddball paradigm was recognizable in all subjects, and had an average latency of 404.1 ± 64.6. The average response time was 382.7 ± 65.49.




EOG-RF (1-RF)
Fz-RF
Cz-RF
Pz-RF
MK-RF (11-RF)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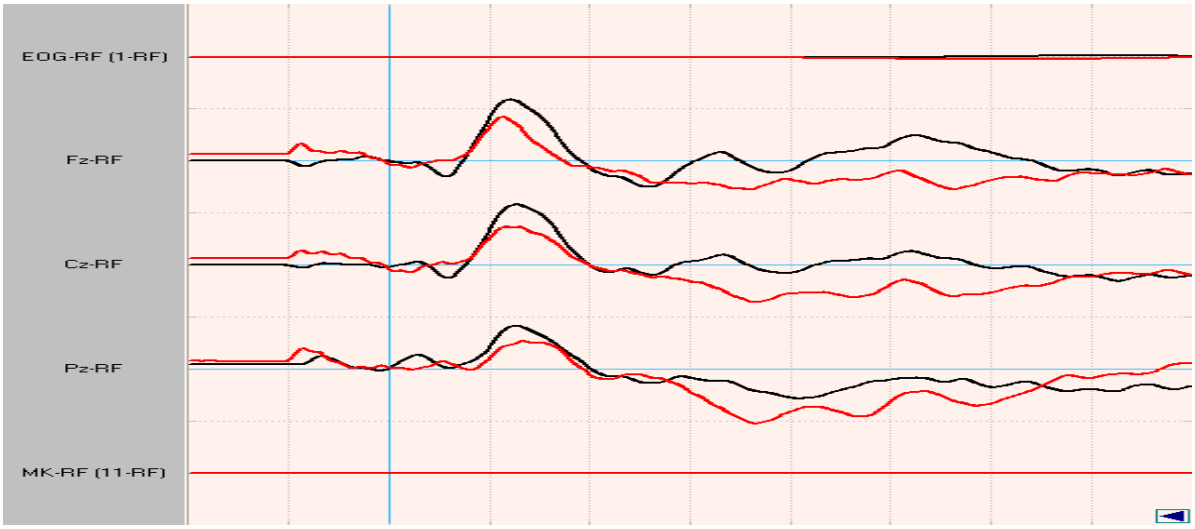
Pz-RF
MK-RF (11-RF)



Discussiom

Contrary to expectations, were not found statistically significant differences between the two groups to the measurements made by DTI in both upper and lower frontal regions.

Our results thus differ with the data in the literature that they encountered in individuals suffering from disorders of impulse discontrollo alterations of frontal white matter less associated with a reduction of the ago and an increase in MD.

MD and are scalar measures that synthesize the carettistiche of the diffusion tensor, a kind of matrix which describes the magnitude and direction of the diffusion of water molecules in the tissues. The pattern of spread may be displayed as a Fresnel ellipsoid with three orthogonal axes of which the length of an axis represents the degree of diffusion. The MD is the free space available for the dissemination, so as to consider the average length of the three axes. It represents the ratio between the length of the primary axis and axes orthogonal, a high value represents a higher orientation of water molecules.

Measurements obtained using DTI are not absolute values and need therefore to be interpreted in context.

In our sample tally in Group Park + ICD of average values more is not associated with reduction of MD (although not statistically significant), may indicate, not so much a specific orientation of the fibers, but, rather, a system, at least from the standpoint of neuro Anatomy, intact.

Neuropsychological assessment results showed no significant differences, if not at the expense of the WCST, indicative of a reduced flexibility and an increase of perseverazioni in patients with ICD. It also remains to report significant differences at the expense of neuropsychological development where scores of the NPI are significantly higher in patients with ICDS, especially in this anxiety, aggressiveness.

This evidence suggests that implausible a parallel between the motor and cognitive characteristics and behavioral. This fits in the context of a current view of Parkinson's disease that includes parallel and progressive involvement of the different systems: the striatal dopaminergic system, mesolimbic and mesocortical (Braak, 2003).

The correlations that emerge between compulsive symptom severity and degree of anxiety and depression configure a psychic situation feature of parkinsoniani patients suffering from ICD we examined. Also, the acknowledgement of a lack of correlation between compulsive symptom severity and overall dosing dopaminergenic, which instead correlates with motor disability, lets assume that this "aberrant" feature behavior may be due to the pathological process of dopaminergic degeneration and perhaps to a lesser extent the influence, undeniable, receptive exogenous stimulation. It should not be forgotten, however, the still unresolved issue discussed and linked to the characteristics premorbose of personality present in each individual as parkinsonian.

Returning to discuss the cognitive aspect of these subjects must focus that despite not having found a picture that lays a cerebral involution pathological, nor an endogenous depressive illness or a picture free of anxiety, it is possible that this disorder may instead be considered in the context of a comprehensive complex associative dysfunction.

Since it is widely credited by literature that specific paradigms of specific elicitano stimulation components that explore "on line" associative functions selective neocorticali, psychophysiology looks a tool particularly suited to study quantitatively selective supplementary activities.

In particular, the study of the Psychophysiological components relative to what is considered elettrofisiologicamente the family of P300, allows you to formulate some consider more about the reply related to decoding and categorization. It is clear that when the trigger or orientation is associated with an operating brain complex task of discriminating power emerge fix obvious, as revealed by increased latency of P3a. The ability of categorization is then quite frankly undermined as demonstrated by increased latency in an oddball paradigm p3b. This seems to be related to the presence of compulsive disorder. However, it should be pointed out as ICD patients, compared to Parkinsoniani without compulsive disorder, P3a monsters lower latency than the P3b, as evident in healthy subjects. The component front, P3a, focused on news of the stimulus, is characterized by a peak latency less than P3b and a maximum amplitude level fronto-Central. Frontal processes involved in dopaminergic p3a are basically (Stanzione 1991). Such evidence would in these patients could be brought into relationship with a relative conservation of potential compared to subjects with only m. Parkinson.

A final point concerns the lack of correlation between degree of motor disability and Psychophysiological data. This could be lead to believe that the physical degeneration is not necessarily scrap with the same intensity of dopaminergic degeneration of the other systems.

In summary, patients suffering from a behavioural disorder related to an aberrant system features mesolimbic, also mesocortical system degeneration as highlighted by the physiological data, to emphasize the intimate anatomical-functional relationship between the two systems to promote and support activities cognitive-behavioral integrative higher order.

In conclusion, parkinsoniani patients with an ICD in the face of an apparent buoyancy retention, cognitive show selective damage of specific functions. The Psychophysiological approach appears suitable for integrated study of cognitive and behavioural functions in their close interrelationship.

The primary limitation of the study is extremely small and clumpy sample; the extension of the case and an adequate selection could, using these methods, characterizing elements morfostrutturali that predispose to the development of the aberrant dopamino related.

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