*Revista de Criminologia e Ciências Penitenciárias*
Conselho Penitenciário do Estado - COPEN
ANO 1 - nº 02
Dezembro/2011



# PSYCHOPATHY AS A DEVELOPMENTAL BRAIN DISORDER: HISTORICAL AND MODERN CONCEPTS AND REVIEW ON BIOLOGICAL EVIDENCE

*Rafael Bernardon Ribeiro* [1]

*Quirino Cordeiro* [2]

---

*1- Médico Formado pela 85ª turma da FMUSP (2002), com residência em Psiquiatria pelo Instituto de Psiquiatria do Hospital das Clínicas da Faculdade de Medicina da USP. Atualmente é médico assistente e pesquisador do IPQ - HCFMUSP nas áreas de terapias biológicas e psiquiatria forense.Aluno do curso de Gestão de Políticas Públicas da EACH-USP (matrícula trancada). Mestrando do Institute of Psychiatry do King's College (London - UK), em psiquiatria clínica forense.*
*2- Diretor do Centro de Atenção Integrada à Saúde Mental (CAISM) da Irmandade da Santa Casa de Misericórdia de São Paulo. Professor Assistente e Chefe do Departamento de Psiquiatria e Psicologia Médica da Faculdade de Ciência Médica da Santa Casa de São Paulo. Membro do Conselho Penitenciário do Estado de São Paulo.*

Resumo

A psicopatia é uma condição que tem intrigado a humanidade há séculos. Seria uma simples questão de falta de moralidade, desvio de caráter e de maldade? Muitos autores importantes discorreram a respeito, como Pritchard, Schneider, Cleckley e Hare, desde o século XIX. O conceito evoluiu, as ferramentas diagnósticas, e os mecanismos biológicos subjacentes. A ciência passa a entender estas pessoas como portadoras de múltiplas disfunções cerebrais, marcadamente no sistema límbico, que justificam seus comportamentos desviados. Destacamos a hipofunção da amígdala, que é responsável pela detecção de medo e tristeza, pelo condicionamento frente a estímulos aversivos, expressão do medo, e leitura ou previsão do comportamento alheio. Estruturas conectadas à amígdala, como o córtex prefrontal medial, cíngulo anterior e lobo temporal não são menos importantes na gênese da condição. Neste artigo, exploramos os aspectos biológicos (neuroimagem funcional e estrutural, genética e função neuronal intrínseca) por trás desta grave condição, que se inicia na infância e segue por toda a vida, causando imensos prejuízos à sociedade.

## Introduction

## The amygdala

The amygdala is a structure formed by grey matter nuclei (rather than an homogeneous structure), localized in deep anterior and medial regions of the temporal lobe, bilaterally. We can name, histologically/anatomically, four main nuclei: central, medial, basolateral and cortical. It's part of the limbic system, along with hyppocampus, parahyppocampus, fornix, entorhinal cortex, cingulate gyrus, thalamus and hypothalamus. It's an ancient structure, fundamental in evolutionary terms as we shall see, and exists in all complex vertebrates. Its general functions are related to fear processing and conditioning, emotion recognition, empathy and memory fixation.[1]

Classically the amygdala was implicated in fear recognition, fear expression, and behavioural conditioning (classical aversive conditioning). There is a vast amount of literature corroborating these findings. Besides this, as new research developed, many connections were found between the amygdala and the prefrontal cortex (medial and orbital areas), bidirectionally. This structure also connects with a series of basal brain structures, like hippocampus, basal ganglia, perirhinal and entorhinal cortices, the basal forebrain, the thalamus and the hypothalamus (in other words, the limbic system), which gives it a far more important role than just fear processing[1,2]. It is particularly important in emotion recognition and attribution of affective valence of stimuli and decision-making based on this valence.

This valence attribution and conditioning can be important to emotion enhanced memory acquisition, as suggested by some neurophysiological studies. Looking in a reversal way, lesions can decrease defensive behaviours (low harm avoidance traits), since this defective brain can not learn an memorize new fearful stimuli as expected normally. So, the amygdala is fundamental to the acquisition of new conditioning towards harmful stimuli.[1, 2]

Regarding the amygdala role in the reward system, new research has shown its role in satiation, or down-regulating the reward reinforced stimulus. Without this particular property, the subject, in experimental settings (monkeys with inactivated amygdala) can not refrain themselves from choosing the stimulus (for example, food), even after satiation (devalued reward). Thus, amygdala is necessary in the process of devaluating a reinforcer. [1]

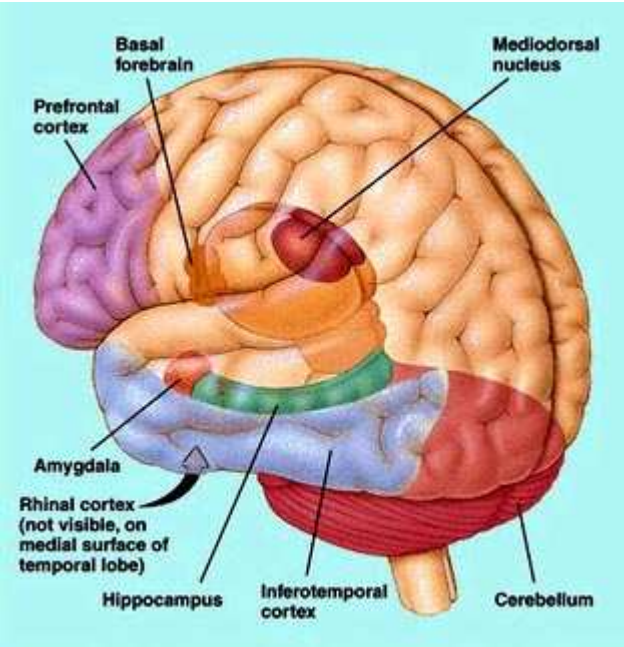
Changing from animal models to human models, a series of paradigms have been developed to test hypothesis related to fear, in functional neuroimaging studies. Using blood-oxygenation level-dependent (BOLD) as a marker of activity, image signals in the amygdalar region shows increased activity both for fearful situation for oneself and to others, suggesting its role as part of the "Theory of Mind" apparatus. Functional MRI has shown its role in learning (conditioning) from fearful situations or stimulus and in extinction of fear learning (reversal learning, when a specific stimulus is no longer harmful) – the same that was found previously in non-human primates. Risk taking behaviour appear to have an influence from this nucleus: in gambling paradigms, the amygdalar activation correlates with the degree of risk aversion.[1,3]

In the last few years a new theory, cited above, has started to gain attention of researcher: mentalization or 'Theory of Mind". Basically, as defined by Brothers, "is the processing of any information that culminates in the accurate perception of the dispositions and intentions

of other individuals"[3]. In other words, its related to our capability and intrinsic biological structures that allows us to understand other people's emotions (based on visual facial and posture pattern recognition) and, in a further and more complex phenomenon, to predict the actions that will take place, based on this emotion recognition. This function is fundamental for social cognition that leads to good social skills and prosocial actions. Seems to be impaired in psychopaths and autistic patients. The amygdala and the limbic system as a whole play a fundamental role in mental states attribution (recognition of expressive gestures and intentional behaviour). Specifically regarding emotional processing, its connection with subgenual anterior cingulate cortex appears to be important to control and suppress, via feedback, the amygdala[14]. It is also suggested to be responsible for processing the emotional content, via aferences from the mirror neuron system, and involved in imitation and recognition of emotions. [3]

Antonio Damasio defines the amygdala as one of the most important structures within the limbic system. Bilateral damage can lead to lifelong emotional impairment, leading to social inadequacy, affective indifference and fear expression or perception impairment[4,5]. Since, for him, all the reasoning and cognition passes through emotion and the "body proper" projections (autonomic outputs from the brain, generating body reactions that will be "read", in a loop, by the brain and will guide our decisions and instincts), this impairment will compromise all our judgement system. So, bodily changes could define an emotion. To feel an emotion, we have to connect an object conscious representation (image) and the emotional body state. The primary (innate) emotions, like fear, anger, sadness, happiness and disgust, depend on limbic structures, particularly on the amygdala and the anterior cingulate gyrus[4]. Since primary emotions are the basis for secondary (more complex, acquired and elaborated)

emotions, without the first, we can't have the second.[4] Damage to the amygdala also makes the patient incapable of recognizing fear in others – and even mentalizing the fear expression. They can not classify faces as trustworthy of not; in other words, they can not make proper social judgements and suffer of excessive trusting behaviour[5].




(image source: http://www.lindenmethodinfo.com/wp-content/uploads/2010/06/amygdala.jpg)

The psychopathy

We can trace back some nosological descriptions of what today we call psychopathy to the XIX century, when James Cowles Prichard (1786-1848), introduced his definition of "moral insanity" in an article published in 1833 in "The cyclopaedia of practical medicine". He stated: "... a form of madness consisting in a morbid perversion of the natural feelings,

affections, inclinations, temper, habits, moral dispositions, and natural impulses, without any remarkable disorder or defect of the intellect or knowing and reasoning faculties, and particularly without any insane illusion or hallucination."[6] The clinical presentation was characterized by "eccentricity of conduct, singular and absurd habits" and "a wayward and intractable temper, with a decay of social affections, an aversion to the nearest relatives and friends formerly beloved,-in short, with a change in the moral character of the individual"[6].The diagnosis was soon accepted by some colleagues of the medical establishment. Of course, it's a broad definition that could encompass a series of different mental disorders, like maniac patients, eating disorders and organic behaviour alterations. Nevertheless, Pritchard has the merit of being one of the first to call attention for personality changes and personality disorders – particularly with antisocial traits.

Another important classical school is the German, centred specifically in Kurt Schneider, professor of Psychiatry in Munich, who wrote "The Psychopathic Personalities", with its first edition in 1923. His definitions were the basis for the ICD – 10 and for the DSM – IV personality categories. At this important book, he defines a man's personality as the combination of "feelings and values, tendencies and volitive dispositions". For him, the many existing personality traits can group randomly in each specific individual, creating a unique person. These traits and consequent personalities are distributed in a "normal" way through the population, generating the "average man". Those personalities that are out of this normal range, are defined as abnormal ones.[7] But, to be a disordered personality, which, by that time, he called "psychopathic", the person must suffer or make suffer. So, "the psychopathic personalities are those abnormal personalities that, for its alterations, suffer or make the society suffer". He created and described 10 categories of "psychopathic personalities":

hyperthymic, depressed, insecure (sensitives and anancasts), fanatical, attention seeking, labile, explosive, affectionless, weak-willed and asthenic. They are very similar to our present classifications. He specifically advised that that they were ideal models, difficulty to find in its pure form in clinical settings[7]. Generally we will find combined traits, and partial forms. The "affectionless" type has an intimate relation with our current definitions of antisocial personality disorders and psychopathy. They were characterized as being unemotional and callous "in face of other human beings"; have no compassion, shameless, no regrets or remorse for their actions, no "moral conscience"; "cold and brutal". They suffer, metaphorically, of moral anaesthesia: "they know perfectly the moral laws; they see them, but don't feel"; "shallow or indiferent in relation to honour, shame, prize and punishment"[7]. So, we can find many similarities to our actual definitions, putting Schneider at the avant-guard of the knowledge by his time. Nowadays, the correct term should be "personality disorder".

After Schneider, narrowing the concept, appears the important book by Hervey Cleckley, in 1941, called "The Mask of Sanity", which is still and interesting descriptive manual[8]. In its beginning the is a particular interesting fable, which I transcript:

"A millionaire notable for his eccentricity had an older and better balanced brother who, on numerous fitting occasions, exercised strong persuasion to bring him under psychiatric care. On receiving word that this wiser brother had been deserted immediately after the nuptial night by a famous lady of the theatre (on whom he had just settled a large fortune) and that the bride, furthermore, had, during the brief pseudo-connubial episode, remained stubbornly encased in tights, the younger hastened to dispatch this succinct and unanswerable telegram:

WHO'S LOONEY NOW? "[8]

This overture is quite symbolic and amazing. Dr. Cleckley calls our attention for the difficulty task of defining sanity and, furthermore, the wide range of nuances that separates lunatics from rational and sane men, in a continuum, rather than a manichean "good and evil" definition. His concerns are towards those who look like sane and competent, but represent "a higher risk to society than those called insane or mentally ill". The name of the book is based on the sanity mask that those individuals show to us, even having an underneath serious behavioural problem, being incapable of having a normal social life. They were not "psychotic or psychoneurotic" - "a challenging enigma" for medical science. He based his work on his clinical experience in asylums and its interface with the justice system. He noticed a set of patients that could not learn from their previous experience, had shallow affect, were parasitic oriented, use of instrumental aggression and were a burden to society. They had in common a deviated pattern of behaviour, tending to disregard moral conventions and laws, tending to exhibit a high degree of maladjustment. He describes 15 cases of his own practice, as examples of the disorder. His sample was biased – he didn't assist deeply perverse and cruel inmates like serial killers or murderers, which were more likely to be in prison, or high functioning corporative psychopaths. Generally his descriptions are of anecdotal and typical patients, who committed copiously minor offences, an where sent back to hospital grounds numerous times, being release always under the promise to behave themselves[8].

Basically, the characteristics are the same as described by Schneider and incorporated in the actual manuals. They were sixteen:

1. superficial charm and good intelligence;
2. absence of delusions and other signs of irrational thinking;
3. absence of nervousness or psychoneurotic manifestations;
4. unreliability;
5. untruthfulness or insincerity;
6. lack of remorse or shame;
7. inadequately motivated antisocial behaviour;
8. poor judgement and failure to learn from experience;
9. pathological egocentricity and incapacity for love;
10. general poverty in major affective relations;
11. specific loss of insight;
12. unresponsiveness in general interpersonal relations;
13. fantastic and uninviting behaviour with drink (and sometimes without);
14. suicide rarely carried out;
15. sex life impersonal, trivial, and poorly integrated;
16. failure to follow any life plan.

The present concept of psychopathy comes from Cleckley and was refined and systematized by the Canadian Psychologist Robert Hare. He states that psychopathy was the first personality disorder described, and the most important for criminal justice[10]. The concept has

been developing for centuries. There are 3 main "clusters": affective, interpersonal, and behavioural attributes. The features for each one are described bellow:

- interpersonally: grandiose, arrogant, callous, dominant, superficial, and manipulative behaviour;
- Affectively: short-tempered, no true emotional bonds with others, lack empathy, guilt, or remorse.
- Lifestyle: irresponsible and impulsive behaviour and a tendency to ignore or violate social and moral convention[10].

The traits are present since childhood and have strong genetic influence. The neuroanatomic substract of these alterations can be grouped in the limbic and paralimbic structures. For their intrinsic features, they are very likely to have problems with criminal justice, but that's not a necessary rule. The most accepted diagnostic tool is Hare's Psychopathy Check-list (PCL-R), which is composed of 20 items, rated from zero to two points (0 for "not present"; 1 for doubt; 2 for certainty). It was designed for use in forensic settings, targeting convicts. Rapidly it has demonstrated to be useful for prediction of recidivism and is widely used in forensic assessments. The evaluation is based on a semi-structured interview and file analysis that will be used to rate the patient. The disorder is stable along the years, and refractory to treatment attempts[10]. The 20 items are: glibness/superficial charm, grandiose sense of self worth, need for stimulation/proneness to boredom, pathological lying, conning/manipulative, lack of remorse or guilt, shallow affect, callous/lack of empathy, parasitic lifestyle, poor behavioural controls, promiscuous sexual behaviour, early behavioural problems, lack of realistic, long term goals, impulsivity, irresponsibility, failure to accept responsibility for own actions, many

short term marital relationships, juvenile delinquency, revocation of conditional release, criminal versatility. They can be divided in two factors (affective/interpersonal and antisocial/criminal lifestyle) and four facets (interpersonal, affective, lifestyle and antisocial). The cut-off varies a little among the different countries and cultures: in Brazil, it's 23; in the UK, 25; and in the USA and Canada, 30 points[11].

Neurodevelopmental aspects of psychopathy

The developmental aspects of psychopathy have drawn attention to the study of children and adolescents with behavioural problems, particularly related to Attention Deficit and Hyperactivity Disorder (ADHD) and antisocial behaviours (conduct disorders – CD)[12, 16]. The subset of patients presenting callous and unemotional (CU) traits in childhood is known to have enhanced likelihood of developing adult psychopathy. The hallmark for the CU subtype is the lack of guilt or empathy[16]. The antisocial personality disorder, psychopathy and conduct disorder are not the same, but there is a clear relationship among them; syndromically speaking there is an overlaping of symptoms, maybe constituting a continuum (from low grade ASPD towards high grade psychopathy) or an evolutionary phase (for conduct disorder in relation to ASPD or Psychopathy). Fact is, most of the psychopaths can be also classified as having antisocial personality disorder (ASPD), being the reversal untrue (only one third of ASPD are psychopaths)[12, 21]. There is a landmark separating the CD children in two different groups, with a very distinct clinical evolution: the callous-unemotional (CU) and the non-callous-unemotional (non-CU)[16]. The manuals, so far, focuse

their polythetic diagnostic criteria in antisocial acts, like aggression, assaults, arson, stealing, lying, criminal justice involvement, problems in maintaining relationships, violence etc. So, it's more focused in expressed behaviour rather than in its underlying causes, inner personal dispositions and affective/emotional fundamental impairments. The manuals (ICD-10 or DSM-IV) still don't separate what appears to be diametrically opposed sub-types: the CU-CD and non-CU-CD, being the same true for ASPD with or without psychopathy. Distinguishing these two groups is important in terms of treatment planning and prognosis evaluation, since the CU patients respond less to interventions and have a worse prognosis[17,18]. They start offending younger, their offences are more violent and they are more likely to be antisocial lifelong, reflecting their lack of empathy[16]. These children, comparing with other children with externalising disorders (like CD or autism), are less distressed by their own behaviour, they are ego-syntonic, and these features facilitate the persistence of antisocial acts (demonstrating problem in moral judgement, which evolves structures as dorsolateral prefrontal cortex and anterior cingulate, this last depending on emotional signalling from the amygdala). In other words, these cited structures, to perform reasoning, decision-making and conflict processing, depend on emotional signalling (and, maybe, bodily emotional projections), to perform their tasks[4]. CU people, having impaired amygdalar function, will fail in moral judgement and will not get distressed by their inadaptative behaviour[5, 16, 17].

The aetiology is not known, but there is a strong suggestion of high genetical influence, being the environment almost negligible in the natural history of CU patients[12, 18]. In one study, a heritability of 67% was found, meaning that the important differences in CU traits found in these children, compared to normal probands, is explained by genetics in one third of the cases [16.]. Giving a reference to compare, the heritability for CD + non-CU is 30%[16].

Blair suggests that classical conditioning (Pavlovian) and instrumental learning are necessary for proper socialisation and acquisition of the necessary skills. So, the humans need to learn from experience, reinforcements and punishments. This population has a great difficulty to learn from past errors and punishment, to process fearful stimuli and to recognize sadness in others[14,18]. As stated before, one of the functions of the amygdala is to process emotions, markedly fear, and to "read" other peoples' emotions and intentions (Theory of Mind). This clinical finding also corroborates with Damasio's theories about feelings and emotions processing. Psychopaths can not have proper somatic representations of emotions, since they have amygdala and prefrontal cortex dysfunction, being unable to feel and to recognize feelings. Their body-mind loop is "broken".[4] This impairment seems to be one of the cornerstones of psychopathy neuropathology. And there is evidence of progressive (developmental) evolution, since only adults with callous-unemotional traits (psychopathy) present orbitofrontal cortex dysfunction, as compared with children[12]. More disturbing is the fact that the emotionally impaired group seem not to respond to adequate and emphatic parenting or good environmental background, leading to a very poor prognosis.[12]

In a 2008 review, Blair also cites the ventromedial prefrontal cortex (which includes anterior and rostral regions of the cingulate gyrus) as an important structure in psychopathy neuropathology[14]. The amygdalar basolateral nuclei are related to operative conditioning (conditioned–unconditioned stimulus associations). These associations are important for controlling its central nucleus, which has projections towards hypothalamic and brainstem structures, controlling behavioural, autonomic and neuroendocrine responses; besides, it is also connected to the ventromedial prefrontal cortex, in a network that commands the decision-making processes[14]. The system is not involved only in aversive conditioning, but

also in positive (appetitive) conditioning. The subgenual anterior cingulate cortex, part of ventromedial prefrontal cortex, receives the emotional inputs from amygdala and the supragenual cingulate cortex controls its activity, suppressing the emotional arousal[14].

Indeed, there is inferential data since the 70's that shows that psychopaths are much less responsive to punishment than to rewarding in cognitive-behavioural attempts of therapy[15]. In a particular observational study with token economy in a prison, when punishment started to be widely used, the drop-out rates grew exponentialy[15]. When the positive reinforcement model was reintroduced, the program started to work again. This corroborates newer studies which have shown that, in psychological treatments for psychopathy, punishment does not work. These findings suggest a link with amygdalar malfunctioning and psychopathy, and maybe there is a qualitative difference between the appetitive and aversive systems, being the first slightly more useful for treatment purposes.

More recent studies, focusing boys with callous–unemotional conduct problems as compared with normal controls have shown increased grey matter concentration in the medial orbitofrontal cortex and the anterior cingulate cortex (both rostrally and dorsally), again pointing to the limbic system[13]. These regions are known to have projections coming and going to the amygdala, and are associated to decision-making, morality, and empathy[1, 12, 13]. In this specific study, no differences in amygdala volume were detected[13]. These structural differences suggest that the orbitofrontal cortex might be associated with poor moral reasoning. However, the specific causes remain unclear. It's suggested that the noradrenergic system could lead to the amygdala dysfunction, since β-blockers (as propranolol) can block the improvement in traumatic memory arousal and can impair the processing of sad facial expressions[12]. Other important neurotransmitters that are involved in regulating aggression

and emotional response are serotonin and dopamine. The first modulates behavioural inhibition and the reward system [22]. Genes controlling the activity of the serotonin transporter (5HTT) and the enzymes monoamine oxidase (MAOA) and catechol-O-methyltransferase (COMT) have been associated to psychopathy. Individuals with low MAOA and 5HTTT were significantly more dysfunctional emotionally and had higher psychopathy scores[23]. High COMT activity was associated just to high emotional dysfunction [23]. These findings suggest that these alterations in serotonergic and dopaminergic neurotransmitter may cause the functional impairment at the amygdala and the PFC [23].

Neuroimaging studies have shown that the degree of psychopathy can be inversely related with the amygdalar volume (f MRI).[12] Raine reported that individual scoring highly on the PCL–R had reduced prefrontal grey, but not white, matter, pointing to another anatomical marker [12]. In a review, strong evidence from neuroimaging was found implicating amygdalar hypofunction (reduced reactivity) and psychopathy (poor emotional processing)[18]. There was also a left amygdala volumetric reduction in one report[18]. Testing reactions to fearful faces in boys with conduct problems (CU+ and CU-), using f MRI, was found just left amygdalar activation, suggesting that CU traits might be linked to low right amygdalar function. Besides this, comparing to normal individuals, the amygdalar function was reduced bilaterally[18]. All these findings in children and adolescents reported above suggest that the hypothesis of psychopathy being a developmental disorder is right[18].

One last study came to our attention, pointing psychopathy as a “disease of the moral brain”[21]. Was suggested that most studies have focused in just a few large structures (temporal cortex and PFC), based on brain injury (“acquired sociopathy”) models. These psychopathic-like patients don't have all the features of the syndrome and there is evidence

that psychopathy is caused by a large number of interconnected and interdependent structures, distributed all over the brain [21]. Based on previous studies, were selected the following areas of interest: basal forebrain-hypothalamus, frontal and temporal poles, superior temporal sulcus region and orbitofrontal cortex. Using voxel-based structural MRI, the study compared ASPD patients (positive for psychopathy using the PCL Search Version) versus normal controls. In the patient's group there were significant volumetric reductions at the frontopolar cortex (left and right), the posterior medial orbitofrontal/ventral subgenual cortex, and superior temporal sulcus (bilaterally).[21] The degree of reductions, as seen in other studies, reflects the severity of psychopathy. Behavioural control and electrodermal response deficits have been related to OFC; the FPC is implicated in long-term planning and reasoning (including in moral tasks); the temporal areas might be involved in semantic cognition and "social reading"/ Theory of Mind tasks; the insula can be associated to somatic/bodily states processing and association with other brain areas; the VMPFC is related to empathy and prosocial acts. So, this is a very unspecific and wider picture, suggesting that the anatomic substract for psychopathy is diffuse and complex[21].

## Conclusion and discussion

If we were to point one single structure implicated in psychopathy aetiology, it would be the amygdala. Is the widely studied (neuroimaging, BOLD, Megneto-Encephalography, f MRI, PET and neuropsychological tests), and almost always found to be dysfunctional in CU

patients. So, the amygdala is one of the main brain structures related to psychopathy, as it encompasses fear perception and processing, stimulus-conditioning behaviours and intention attribution (mentalization). So far, we can argue that psychopaths have all these functions impaired, pointing to the amygdala as the responsible. They show important failure in learning from aversive or appetitive stimulus, (not forming stimulus–reinforcement associations) they don't respond to emotional expressions, like fearful and sad ones, all of these processes being fundamental for socialization and adaptation. Not learning from negative experiences and that some attitudes are bad, they are much more prone to use antisocial and predatory strategies when interacting[14,18]. The psychopaths also have less or no autonomic reactions when prepared/instructed about a future fear situation. This normal reaction is mediated by amygdalar activation[14]. Another finding is the fact that these patients are less influenced by emotional distracters in experimental models, another role played by amygdalar function. But, we can not ignore that the amygdala is part of a very complex system of interconnected limbic structures (prefrontal cortex, as the ventromedial region, cingulate gyrus, hippocampus, etc)[12,14,18]. All these structures have a core role in emotion processing, moral judgement, impulse control[17]. The ventromedial prefrontal cortex, in particular, appears to be very important in regulating amygdalar activity (negative feedback after arousal, from anterior cingulate)[18]. Besides this, another paper from this author shows that psychopaths have semantic and language impairments (they can not couple semantic and emotional representations), demonstrating that there are other domains, such as temporal and parietal lobes, might be involved in psychopathy pathology (or its connections with the limbic system and prefrontal cortex)[19]. Damasio's theories, implicating bodily emotional (somatic) reactions as important part of emotional processing, are also interesting and can be part of the

puzzle[4] . Neuropsychological tests in patients with amygdala damage shows fear and sadness processing impairment and deficits in conditioning learning, the same findings in CU patients [18]. They also show reduced eye gaze to the interlocutor eye, observation seen as a partial explanation for the impairment in emotion (fear or sadness) recognition, needing further investigation[14].

Concluding, the two core regions related to psychopathy so far are both the amygdala and the ventromedial prefrontal cortex. It'll be difficult to dissociate them, since they work together and both appear to be hypofunctional in brain imaging studies [14,18,20]. It's a neurodevelopmental brain disfunction/disorder that is present since childhood (functionally, anatomically and in expressed behaviour), and that probably progresses as growth takes place [16, 18, 21]. The investigation of biological markers (genetic and structural/functional brain imaging) is necessary to detect the underlying causes and will be a starting point to new precocious treatment and preventive measures still in childhood.

REFERENCES:

[1]Morrison SE, Salzman CD. Re-valuing the amygdala. Curr Opin Neurobiol. 2010 Apr;20(2):221-30. Epub 2010 Mar 17

[2]Maren S. Pavlovian fear conditioning as a behavioral assay for hippocampus and amygdala function: cautions and caveats. Eur J Neurosci. 2008 Oct;28(8):1661-6.

[3]Mier D, Lis S, Neuthe K, Sauer C, Esslinger C, Gallhofer B, Kirsch P. The involvement of emotion recognition in affective theory of mind. Psychophysiology. 2010 Nov;47(6):1028-39

[4]Damasio A. Descartes' Error. Vintage Books, 2006.

[5]Damasio A. The feeling of what happens. Vintage Books, 2000.

[6]Augstein HF. J C Prichard's concept of moral insanity--a medical theory of the corruption of human nature. Med Hist. 1996 Jul;40(3):311-43.

[7]Schneider K. Las Personalidades Psicopáticas. 2.a Edición. Ediciones Morata, Madrid, 1948.

[8]Cleckley H. The Mask of Sanity. Fifth Edition, 1988.

[9]Kaplan & Sadock. Synopsis of Psychiatry. 10th Edition, Lippincott Williams & Wilkins, 2007.

[10]Hare RD. Psychopathy: a clinical and forensic overview. Psychiatr Clin North Am. 2006 Sep;29(3):709-24. Review.

[11]Hare RD. Hare Psychopathy Checklist-Revised (PCL-R) manual. 2nd Edition, MHS.

[12]Blair RJ. Neurobiological basis of psychopathy. Br J Psychiatry. 2003Jan;182:5-7.

[13] [1]: De Brito SA, Mechelli A, Wilke M, Laurens KR, Jones AP, Barker GJ, Hodgins S, Viding E. Size matters: increased grey matter in boys with conduct problems and callous-unemotional traits. Brain. 2009 Apr;132(Pt 4):843-52. Epub 2009 Mar 17.

[14]Blair RJ. The amygdala and ventromedial prefrontal cortex: functional contributions and dysfunction in psychopathy. Philos Trans R Soc Lond B Biol Sci. 2008 Aug 12;363(1503):2557-65.

[15]Bassett JE, Blanchard EB. The effect of the absence of close supervision on the use of response cost in a prison token economy. J Appl Behav Anal. 1977 Fall;10(3):375-9.

[16]Viding E, Blair RJ, Moffitt TE, Plomin R. Evidence for substantial genetic risk for psychopathy in 7-year-olds. J Child Psychol Psychiatry. 2005 Jun;46(6):592-7.

[17]Greene JD, Nystrom LE, Engell AD, Darley JM, Cohen JD. The neural bases of cognitive conflict and control in moral judgment. Neuron. 2004 Oct 14;44(2):389-400.

[18]Jones AP, Laurens KR, Herba CM, Barker GJ, Viding E. Amygdala hypoactivity to fearful faces in boys with conduct problems and callous-unemotional traits. Am J Psychiatry. 2009 Jan;166(1):95-102.

[19]Blair KS, Richell RA, Mitchell DG, Leonard A, Morton J, Blair RJ. They know the words, but not the music: affective and semantic priming in individuals with psychopathy. Biol Psychol. 2006 Aug;73(2):114-23.

[20]Marsh AA, Finger EC, Mitchell DG, Reid ME, Sims C, Kosson DS, Towbin KE, Leibenluft E, Pine DS, Blair RJ. Reduced amygdala response to fearful

[21]de Oliveira-Souza R, Hare RD, Bramati IE, Garrido GJ, Azevedo Ignácio F, Tovar-Moll F, Moll J. Psychopathy as a disorder of the moral brain: fronto-temporo-limbic grey matter reductions demonstrated by voxel-based morphometry. Neuroimage. 2008 Apr 15;40(3):1202-13. Epub 2008 Jan 11.

[22]Völlm B, Richardson P, McKie S, Reniers R, Elliott R, Anderson IM, Williams S, Dolan M, Deakin B. Neuronal correlates and serotonergic modulation of behavioural inhibition and reward in healthy and antisocial individuals. J Psychiatr Res. 2010 Feb;44(3):123-31.

[23]Fowler T, Langley K, Rice F, van den Bree MB, Ross K, Wilkinson LS, Owen MJ, O'Donovan MC, Thapar A. Psychopathy trait scores in adolescents with childhood ADHD:

the contribution of genotypes affecting MAOA, 5HTT and COMT activity. Psychiatr Genet. 2009 Dec;19(6):312-9.