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Caudate nucleus and social cognition: Neuropsychological and SPECT evidence from a patient with focal caudate lesion

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ABSTRACT

Keywords:

Caudate nucleus
Theory of Mind
Social cognition
Emotion

Most studies in social cognition have focused on developmental diseases or analyzed the consequences of acquired frontal lesions on the integrity of Theory of Mind (ToM), but, to our knowledge, none to date has addressed the eventual consequences of damage to the basal ganglia on ToM. To investigate the possible consequences of such lesions on social cognition, we tested a selected patient, MVG, a 44-year-old man with a focal caudate nucleus (CN) lesion following stroke. In the aftermath of this stroke, MVG shows loss of empathy and difficulties recognizing emotions in others. The dual aims of this study were first, to evaluate the implications of CN on ToM and recognition of emotion, and second, to discuss these results as a consequence of a disconnection of the sub-cortical orbito-frontal (OF) loop due to caudate damage. We performed a complete neuropsychological assessment of MVG, as well as different tasks evaluating social cognition, such as the Faux-Pas Test and the Reading the Eyes in the Mind Test. No deficits were found in the neuropsychological tests. However, on tasks assessing social cognition, MVG showed impairments in the “warm” or “affective” part of ToM as well as in the ability to recognize negative emotions (i.e., sadness and fear). These results indicate that damage to the head of the left CN can lead to impairment of ToM and emotion recognition. Furthermore, the data shows that, in MVG, such impairment appears to be due to a disconnection of the sub-cortical OF circuit resulting from damage to the CN. Neuro-imaging data tends to confirm this hypothesis by bringing out a hypo-perfusion in both, the territory of his left CN and prefrontal (i.e., ventromedial) brain areas.

1. Introduction

The basal ganglia (BG) (i.e., striatum, globus pallidus, substantia nigra, sub-thalamic nucleus) are involved in the regulation of

motor functions, motivation and procedural learning (Graybiel et al., 1994; Yin and Knowlton, 2006), as well as in cognitive functioning, behavior and personality (Abdullaev et al., 1998; Laplane et al., 1989), with the striatum, an important part of

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the BG, involved in affective processes. The striatum can be divided into the ventral striatum, which contains the nucleus accumbens, and the dorsal striatum, which contains the caudate and putamen (Utter and Basso, 2008). Lesions in the caudate nucleus (CN) are most likely to cause behavioral alterations (Bhatia and Marsden, 1994), as well as cognitive losses in Huntington's disease (Lawrence et al., 1998) and Parkinson's disease (Rinne et al., 2000), and possibly also in obsessive compulsive disorder (Baxter, 1992). Lesions in the CN have been associated with a wide range of behavioral alterations, including abulia (Trillet et al., 1990), disinhibition, a variety of affective and personality disorders (Kumral et al., 1999) and depression (Caplan et al., 1990), suggesting that the sequelae of CN damage are not always homogeneous among patients. However, a consensus has been established concerning the behavioral and cognitive consequences of CN damage, which appear commonly in the foreground.

The BG are thought to be connected to well delimited regions of the frontal cortex by five separate and parallel loops (Alexander et al., 1986). Two of these loops connect the CN to frontal neocortical regions of the brain, which have been implicated in higher cognition; these loops are the dorsolateral (DL) loop, which regulates executive functions and involves the DL part of the head of the CN, and the orbito-frontal (OF) circuit, which mediates affective processes and involves the ventro-medial part of the caudate. On the basis of the model of these fronto-sub-cortical circuits, detailed predictions have been made regarding the causal relationship between specific behavioral consequences and the disruption of a particular loop (Lawrence et al., 1998; Mega and Cummings, 1994). Behavioral disturbances following damage to the CN seem to result from an impairment of function in cortical areas, due to a loss of striatal efferences from the CN (Kumral et al., 1999). That is, these behavioral disturbances result from the disturbances in connectivity among cortico-sub-cortical networks due to damage to the BG. A description of two patients supports this hypothesis (Benke et al., 2003). Indeed, from a phenomenological perspective, the observed behavioral (i.e., abulia) and cognitive (i.e., executive functions) modifications since stroke would be consistent with a disruption of the anterior cingulate-prefrontal and the DL prefrontal circuits, respectively.

Hence, if impairment of one of the BG pertaining to one of these circuits induces deficits similar to those caused by a lesion of the cortical area belonging to that loop, there may also be consequences of this impairment in another domain, namely social cognition. Indeed, the prefrontal cortex (PFC), comprising the orbito-frontal cortex (OFC), has been shown to play an important role in social cognition (Adolphs, 1999).

Social cognition alludes to the processes by which we make sense of ourselves, the social environment in which we live and the individuals around us (Fiske, 1993; Macrae and Bodenhausen, 2000) and the ability to represent internal somatic states, knowledge about the self, perceptions of others and interpersonal motivations which are carefully orchestrated to support skilled social functioning (Fiske and Taylor, 1991). It refers to a relatively large number of constructs. The most representative mechanism of social cognition is Theory of Mind (ToM), which alludes to a skill that underlies humans' ability to engage in complex social interactions: the ability to make

inferences about others' mental states. Within ToM, there is both a cognitive or "cold" component and an empathic, affective or "warm" component (Coricelli, 2005). Cognitive ToM refers to the ability to make inferences about the cognitive states, beliefs, thoughts, intentions and motivations of other people (Brothers and Ring, 1992; Coricelli, 2005), while affective ToM refers to the ability to infer the feelings, affective states and emotions of others (Brothers and Ring, 1992). Furthermore, the neuronal bases underpinning affective and cognitive ToM seem to be different, suggesting that cognitive and affective mentalizing abilities are partly dissociable (Shamay-Tsoory and Aharon-Peretz, 2007).

Empathy, a second component of social cognition, is mainly implicated in prosocial behavior, morality and the regulation of aggression (Eisenberg and Eggum, 2009). Moreover, the term empathy is applied to a broad spectrum of phenomena, from feelings of concern for other people that create a motivation to help them, experiencing emotions that match another's, knowing what the other is thinking or feeling, to blurring the line between self and other (Hodges and Klein, 2001). Empathy is not a passive affective resonance phenomenon with the emotions of others. Rather, goals, intentions, context and motivations play feed-forward roles in how emotions are perceived and experienced. According to a recent model, empathy can be separated in two systems, which are affective empathy (i.e., the capacity to *experience* affective reactions to the observed experiences of others) and cognitive empathy (i.e., *making inferences* regarding the other's affective and cognitive mental states) (Shamay-Tsoory, 2010), which can be impaired selectively [e.g., (Dziobek et al., 2008)]. The term "empathy" as used in this study only alludes to affective empathy, since cognitive empathy refers to ToM.

The recognition of emotions in faces is also an essential component of social cognition. Facial expressions signal important information about the internal states of others and the external events that may have elicited those expressions (Ekman, 1997). Individuals use this information to guide their social behavior.

Many studies have enabled identification of the cerebral areas implicated in ToM. The social cognition tests used in this study have frequently been used in functional neuro-imaging and lesion studies in order to enable identification of the cerebral areas implicated in ToM.

For example, a popular paradigm of ToM assessment in neuro-imaging studies consists in using false-belief tasks [inspired by (Happé et al., 1998) task; see below for a task description] during functional magnetic resonance imaging (fMRI) measures. Indeed, this paradigm has shown that the medial PFC [e.g., (Saxe and Wexler, 2005)], more precisely Brodmann areas 8 and 9, plays a crucial role in this ability in healthy adults [e.g., (Fletcher et al., 1995; Russell and Sharma, 2003)]. Implication of other brain areas such the right lateral rostral PFC has also been objectified by this type of paradigm [e.g., (Sommer et al., 2007)]. A study using event related potentials provided further evidence for the involvement of the left frontal areas in achieving this task (Sabbagh and Taylor, 2000). Furthermore, the Faux-Pas Test is a popular test of ToM assessment in lesion studies. Indeed, it has highlighted impairment of this ability in patients with lesions

in the medial PFC [e.g., (Geraci et al., 2010)], and more precisely the OFC [e.g., (Shamay-Tsoory and Aharon-Peretz, 2007)]. Moreover, another test, frequently used in order to evaluate the ability to infer mental states to others is the Reading the Mind in the Eyes (RME) Test. The involvement of the medial prefrontal cortex (mPFC) in this ability was highlighted by a study of event related potentials (Sabbagh et al., 2004) and lesion studies [e.g., (Geraci et al., 2010)]. Another aspect of social cognition, namely the ability to recognize emotions in others is frequently assessed with a range of photographs from a series of Pictures of Facial Affect (Ekman and Friesen, 1976). For example, studies using this test have reported that the amygdala appears to play a core role in this ability [e.g., (Breiter et al., 1996; Fitzgerald et al., 2006)]. Other cerebral areas, such as striatal regions [e.g., (Calder et al., 2003; Sprengelmeyer et al., 2003)] and the OFC [e.g., (Blair and Cipolotti, 2000; Heberlein et al., 2008)] have also been shown to be implicated in emotion recognition. Interesting findings have also been reported by (Blair and Cipolotti, 2000). Using the social situations and a moral/conventional distinction tasks, they found that damage to the right frontal region, including the OFC, result in severe impairment in the judgment of moral and conventional transgression, as well as in the identification of social violations.

Most studies of social cognition have involved developmental diseases, such as autism and Asperger's syndrome [e.g., (Baron-Cohen et al., 1999; Kaland et al., 2008; Spek et al., 2010)] or have analyzed the consequences of acquired frontal lesions on the integrity of ToM [e.g., (Shamay-Tsoory et al., 2009, 2006, 2005; Stone et al., 1998; Stuss and Anderson, 2004)], but, to our knowledge, none to date has addressed the consequences of damage to the BG on ToM.

Although some studies assessed, and highlighted, the implication of CN in social decision-making tasks, such as altruistic punishment [e.g., (de Quervain et al., 2004; Strobel et al., 2011)], norm compliance [e.g., (Spitzer et al., 2007)] and reactive aggression [e.g., (Mendez et al., 2011)], most studies assessing the consequences of CN lesions have focused on behavioral and motor disturbances and cognitive deficits (e.g., language, memory, executive functions). Nevertheless, given the neural correlates underpinning social cognition, and especially the medial PFC [e.g., (Blair and Cipolotti, 2000; Geraci et al., 2010; Heberlein et al., 2008; Sabbagh et al., 2004; Saxe and Wexler, 2005; Shamay-Tsoory and Aharon-Peretz, 2007)], assessment of these abilities following BG damage, in the light of the theory of fronto-sub-cortical circuits, appears of particular interest.

We describe the behavioral and neuropsychological impairments in one subject who suffered a vascular lesion of the left CN. Special emphasis was placed on social cognition, including a comprehensive assessment of ToM and emotion recognition. Therefore, the aim of this study was to examine the involvement of the CN in ToM, empathy and emotion recognition, by performing a detailed study of a selected patient with a focal CN lesion. We also sought to analyze in detail the relationship between the behavioral pattern in this patient and his underlying CN lesion. From these results, we attempted to clarify how well the observed impairments are compatible with the postulated alterations, as predicted by the theory of fronto-sub-cortical loops, especially in the

domain of social cognition. Thus, based on findings regarding the neuro-anatomic correlates of ToM, we formulated two hypotheses: (1) a focal lesion of one BG will result in disturbances in social cognition and (2) these disturbances in the domain of social cognition will be a consequence of a disconnection of the sub-cortical OF circuit caused by the BG lesion.

2. Methods

2.1. Case history

In February 2006, MVG, a 44-year-old man, was admitted to the Neurology Department of Hôpitaux Civils de Colmar. He was diagnosed with an arterio-venous malformation of the head of the left CN in a hemorrhagic stage and treated by radio-surgery (Gamma-Knife) a few months later. An MRI performed in April 2010 showed sequelae in the territory of the dorso-medial part of the head of the left CN and, to a lesser extent, in the neighboring part of the anterior limb of the internal capsule and the putamen (Fig. 1).

Approximately 5 months after the stroke, MVG and his family noticed changes in his behavior and mood, including marked irritability and mood swings leading to relational tensions. MVG described himself as someone who “became selfish”, who “did not have any feelings anymore” (e.g., he became insensitive to his daughters' crying). Furthermore, he cut ties with his friends, saying he “does not need them anymore”. His restlessness and impulsiveness were accompanied by a permanent inner tension. As stated by his wife, MVG became “paranoid” and “mean”, although he had been rather introverted before the stroke.

Moreover, MVG described difficulties in recognizing emotions in others especially negative emotions and he had problems interpreting others' facial expressions. However, he could still feel positive and negative emotions, with his expression of positive emotions even enhanced.

Cognitively, MVG complained minimally about concentration difficulties and very slight perturbations of memory. Summaries of assessments of intelligence, memory, executive functions, language, attention and perception are shown in Table 1.

Assessment by the Wechsler Adult Intelligence Scale - third edition (WAIS-III) showed that MVG had a full scale Intelligence Quotient (IQ) of 85 [Verbal Intelligence Quotient (VIQ) 77, Performance Intelligence Quotient (PIQ) 98]. His abstract reasoning, as determined by Raven's Progressive Matrices, was excellent. Furthermore, there was no evidence of impairments in his memory, language, visual attention or visual perception. Although two of the executive functions measures appear to be below average, they objectify a slowdown (i.e., Stroop test), rather than real executive function deficits. Similarly, the Rey-Osterrieth Complex Figure being copied successfully, and MVG's performances on the Tower of London Test being excellent, planning difficulties in MVG can be excluded. Hence, the only slowdown highlighted by the neuropsychological assessment is not likely to interfere with the performances on the social cognition tasks.

Preceding the stroke, MVG had no history of psychiatric or neurological antecedents.

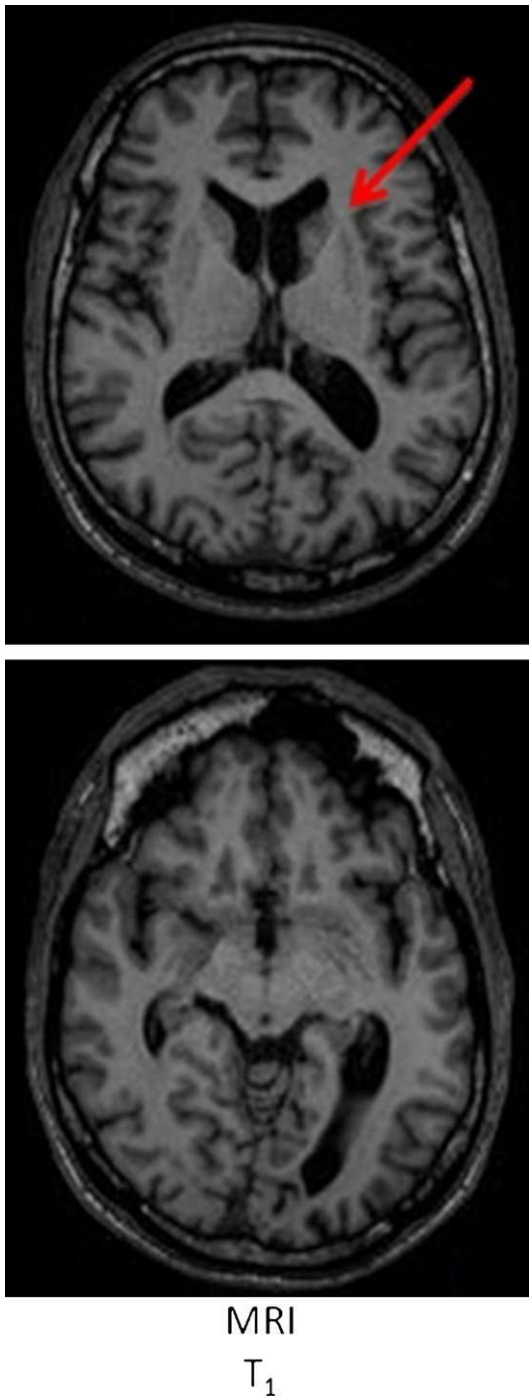


Fig. 1 e Transverse slices showing T1-weighted MRI: the MRI shows focal low signal intensity sequelae of gamma-knife radio-surgery of left CN (red arrow).

In the aftermath of the stroke, three consecutive cerebral angio-MIRs was performed in 2006, 2007 and 2008 highlighting “an arterio-venous malformation, mainly driven by the artery of Heubner and secondarily by perforating arteries from the M1 segment of the left middle cerebral artery, with a rather diffuse nidus” and “the persistence of a discrete afferent of the CN”. MVG further had a neuropsychological testing in 2007, pointing out difficulties in recognizing emotions and, in

a much lesser extent, an attention deficit. His memory and executive functions were preserved. Although the complaint about behavioral modifications (e.g., loss of empathy, irritability) was on the foreground, this aspect has not been further assessed in 2007.

MVG provided informed consent to participate in this study. Follow-up assessments for this study were performed on several occasions from December 2009 to April 2010.

2.2. Control participants

Twelve healthy volunteers (males), matched in age (mean SD age, 44.8 2.5 years) and education level (11 years of education), all native French speakers, served as controls. Subjects with a history of neurological or psychiatric disorders were excluded.

2.3. Social cognition tasks

2.3.1. Recognition of Faux-Pas

Participants were orally administered the French version of the Faux-Pas Test (Baron-Cohen et al., 1999; Cohen et al., 2006). This test, assessing, both the “cognitive” and the “affective” parts of ToM, consists of 20 short stories, 10 with and 10 without a Faux-Pas. Indeed, although test requires understanding the knowledge of others, it is also supposed to require in addition an empathic appreciation of their emotional state. A Faux-Pas occurs when someone says something they should not have said, not knowing or not realizing that they should not say it. To understand that a Faux-Pas has occurred, an individual has to represent two mental states: that the person saying it does not know that he or she should not say it and that the person hearing it would feel insulted or hurt. In other words, understanding a Faux-Pas requires understanding both a mental state of belief or knowledge and having some empathic understanding of how the person in the story would feel. Thus there is both a cognitive component and an empathic affective component. Once read, the stories remained in front of the participant while questions were asked, to reduce memory demands. Each story had two types of questions, that is six ToM questions: (1) did someone say something they shouldn’t have said? (tests detection of Faux-Pas), (2) who said something they shouldn’t have said? (tests understanding of Faux-Pas), (3) why shouldn’t they have said it? (requires understanding of the mental state of the listener) (4) why did they say it? (requires understanding of the mental state of the speaker) (5) did X know that Y - ? and (6) how do you think Y felt? and two control (non-ToM) questions.

2.3.2. First- and Second-Order False-Beliefs Tasks

Participants were orally administered a French version of the First- and Second-Order False-Beliefs Tasks (Ehrle et al., 2011). These tasks were designed to test subjects’ ability to make inferences about another person’s *mental* state (i.e., “cognitive” or “cold” part of ToM). The stories were inspired by those from previous studies (Baron-Cohen et al., 1985; Wimmer and Perner, 1983). First-order False Beliefs Tasks were designed to test a subject’s ability to infer that someone may have a mistaken belief that is different from that subject’s own true belief, or, in other words, the ability to infer mental states of

Function	Test	Detail	Scores
Intelligence	WAIS-III	Full scale IQ	85
		VIQ	77
		PIQ	98
	Progressive Matrices 38 (PM 38)		46/60
Memory	Rappel Libre/Rappel Indices-16 (RL/RI-16)	Immediate recall	16/16
		Free recall	7-10-13/16
		Total recall	14-16-16/16
		Recognition	16/16
		Differed free recall	12/16
		Differed total recall	16/16
	Rey complex figure	Immediate recall	18.5/36
		Differed recall	19.5/36
	Delayed matching to sample-48 (DMS-48)	Set 1	99%
		Set 2	99%
	Verbal span	Forward order	5
		Reverse order	4
	Visual span	Forward order	10
Reverse order		6	
Executive functions	Frontal Assessment Battery (FAB)		17/18
	Trail Making Test (TMT): time (sec)	A	24
		B	62
	Stroop	Reading	79*
		Denomination	60*
		Interference	41
		Interference score	66.9
	Rey complex figure e copy	Planification	Type IV*
		Time	2'06
		Score	34/36
	Verbal fluency (1 mm)	Literal	11
		Semantic	21
	Cognitive estimations		15/15
	Tower of London	Success in less than 60 sec	12/12
		Score	29/36
	Modified Card Sorting Test (MCST)	N° of categories	6/6
		N° of cards	36
		N° of errors	0
		N° of perseverations	0
		Total score	-2
	Iowa gambling task	Bloc 1	4
		Bloc 2	0
		Bloc 3	-4
Bloc 4		-2	
Bloc 5		0	
Language	DENO-100		100/100
Attention	Mesulam symbol cancellation test (SCT) (A)	Organized	0 omission 69 ⁰⁰
		Randomized	0 omission 98 ⁰⁰
Perception	Face recognition	Short form	23/27
		Long form	47/54
	Mutual gaze detection	% of correct answers	89.58
		Eccentricity: 0°	91.66
		Eccentricity: 5°	66.66
		Eccentricity: 10°	100
Eccentricity: 15°	100		

NB: pathological scores (at 1.65 SD, scores below pathological threshold or below cut-off) are marked by an asterisk (*).

the type “A thinks X”. These tasks require consideration of only one character’s perspective. False-belief tasks typically involve one person putting an object somewhere in the presence of another person and then leaving the room. The second person moves the object to another location while the first person is away. The first person returns, and the subject is asked three questions: (1) the “belief question”, which asks where the first person thinks the object is, thus requiring an understanding of others’ mental states; (2) the “reality question”, which asks where the object really is; and (3) the “memory question”, which asks where the object was at the beginning. Second-order False Belief Tasks were designed to test the ability to understand what someone else thinks about what another person thinks. In each story, Person 1 places an object somewhere and then leaves the room. Person 2 moves the object. While Person 1 is out of the room, he or she peeks back in and sees the object being moved, but Person 2 does not know that Person 1 has seen this. The subject is asked, “When Person 1 comes back in, where will Person 2 think that Person 1 thinks the object is?”

2.3.3. RME Test

Participants were administered the French version of the “RME” test, which has been described in detail (Baron-Cohen et al., 2001). This test evaluates the ability of an individual to determine the mental state of another individual by looking at a picture of the latter’s eyes (i.e., the visual side of ToM). The task consists of 36 items, showing the eye region of black and white photographs of 36 different faces, both male and female. Each picture has four mental state terms printed below it, and the participant has to choose the word that best describes what the person on the photograph is feeling or thinking. During the test, participants had the possibility to consult a glossary containing synonyms and examples of each word to ensure their comprehension of that word.

2.3.4. Emotion recognition

Emotion recognition has been assessed using a range of photographs from a series of Pictures of Facial Affect (Ekman and Friesen, 1976). From this series, we chose the faces of 10 actors (five females, five males), each displaying six basic emotions (i.e., happiness, sadness, disgust, fear, surprise and anger) and a neutral facial expression. Upon looking at each photograph, participants chose the emotion (i.e., happiness, sadness, disgust, fear, surprise, anger or neutral) that best corresponded to his opinion of that facial expression. The maximum score, indicating best performance, was 10 for each facial expression. The photographs were presented to each subject in a random order.

2.3.5. Moral and Conventional Judgments

The Moral and Conventional Judgments Test [e.g., (Blair, 1995; Turiel et al., 1987)] evaluates the comprehension of social rules that can be moral (i.e., victim-based) or conventional (i.e., social disorder-based) (Blair and Cipolotti, 2000). A French version of this test (Ehrle et al., 2011) was presented to the participants. The participants were read short scenes describing which children frequently do at school; 10 scenes describe moral or conventional transgressions (e.g., “One child runs up to another child and hits them in the face” and “One

child stands up and walks straight out of the classroom without permission in the middle of the lesson”, respectively). Three questions were asked: (1) was it right or wrong for X to do Y?; (2) on a scale of one to 10, how right (or wrong, depending the answer to 1) was it for X to do Y?; (3) now what if the teacher said before X did Y, that ‘At this school anybody can do Y if they want to’ would it be O.K. for X to do Y if the teacher says X can?

2.3.6. Social Situations

The Social Situations Test (Dewey, 1991), assesses the comprehension of social permissibilities and the ability of judgment concerning the appropriateness of behaviors that may induce anger or irritation in observers, has been described in detail (Blair and Cipolotti, 2000). A French version of this test (Ehrle et al., 2011) was presented to the participants, who had to read short stories describing either normative or inappropriate behavior. Several times, the participant was asked to indicate whether he thinks the behavior is appropriate or not.

2.3.7. Scales and questionnaires

Depression and anxiety were assessed using the Beck Depression Inventory (BDI): (Beck and Beck, 1972), French version, (Delay et al., 1963) and the State-Trait-Anxiety-Inventory (STAI): (Spielberger, 1983), French version, (Bruchon-Schweitzer and Paulhan, 1993), respectively.

To assess additional information regarding MVG’s behavioral modifications since his stroke, he was administered various scales and questionnaires, including the 20-item Toronto Alexithymia Scale (TAS-20), (Bagby et al., 1992); French version, (Loas et al., 1995); the Social Anhedonia Scale (SAS), (Eckblad et al., 1982); French version, (Kosmadakis et al., 1995); the Empathy Quotient (EQ), (Baron-Cohen and Wheelwright, 2004); French version, (Weiner et al., not published); the Temporal Experience of Pleasure Scale (TEPS), (Gard et al., 2006); French version (EETP), (Loas et al., 2009); and the Patient Competency Rating Scale (PCRS), (Prigatano et al., 1986).

2.3.8. Complementary evaluations

We interviewed MVG’s wife to acquire more qualitative information about his behavioral and mood modifications following his stroke. Furthermore, we administered the Iowa Rating Scales of Personality Change (Barrash et al., 1997) French version, (Juillerat & Peter-Favre, not published) to MVG’s wife to quantify these modifications. Thirty “clinical scales” assess disturbances various aspects of personality and behavior. Each behavioral characteristic is defined briefly. The listing is based on a seven-point scale (a rating of one reflects excellent behavior; a rating of three is average; a rating of five reflects a moderate disturbance; a rating of seven reflects severe disability). MVG’s wife rated the current level of each item and her husband’s behavior during the 6 months preceding surgery with the same scale. The difference between the two ratings provides a measure of the extent of the changes. This scale has been described in detail (Houeto et al., 2002).

3. Results

To compare MVG’s performances with those of the control participants, we used the non-parametric Crawford and

Howell (1998) test (modified *t*-test) for all of the social cognition tasks.

3.1. Social cognition tests

Performances of MVG and the control subjects on the Faux-Pas, the First- and Second-Order False Belief, the RME and the Social Situations tests are shown in Table 2.

On stories without a Faux-Pas of the Faux-Pas Test, MVG's score did not differ significantly from controls' scores. MVG's score was identical to controls' scores on control questions for which both achieved maximal scores. On stories with Faux-Pas, MVG's scores on the questions relating to faux pas were significantly poorer than the scores obtained by the control subjects ($t \frac{1}{4} -7.17, p < .01$). A detailed analysis showed that MVG detected significantly fewer faux pas than the controls ($t \frac{1}{4} -3.18, p < .01$). The percentage of correct responses to the six questions related to each story was computed only for correct stories in which faux pas were detected. MVG had significantly lower scores compared with controls for three of the six questions ($t \frac{1}{4} -5.29, p < .01$; $t \frac{1}{4} -1.88, p \frac{1}{4} .04$ and $t \frac{1}{4} -2.96, p \frac{1}{4} .01$, respectively) (Fig. 2). Both MVG and the control participants obtained maximal scores for the control questions.

There were no significant differences between MVG and the control group on both the First ($t \frac{1}{4} -.65, p \frac{1}{4} .26$) and Second ($t \frac{1}{4} -.56, p \frac{1}{4} .29$) Order False Belief Tasks.

MVG scored significantly lower than the control group ($t \frac{1}{4} -5.44, p < .01$) on the RME Test.

Furthermore, MVG had a normal total score on the Emotion Recognition Test, as well as normal scores for neutral facial expressions, expressions of happiness, disgust, surprise and anger, but his scores for facial expressions of fear and sadness were 2 standard deviation (SD) and 2.152 SD, respectively, below the normal range.

The maximal scores were achieved by MVG on the Moral (15/15) and Conventional (15/15) Judgments Tasks.

MVG's scores on both appropriate and inappropriate situations, as well as his total score on the Social Situations Test, were lower than those of the controls. However, none of these differences reached statistical significance ($t \frac{1}{4} -1.15, p \frac{1}{4} .13$, $t \frac{1}{4} -1.02, p \frac{1}{4} .16$ and $t \frac{1}{4} -1.72, p \frac{1}{4} .06$, respectively).

3.2. Scales and questionnaires

The BDI and the STAI showed that MVG had signs of both depression and anxiety. Moreover, MVG showed signs of alexithymia, in particular difficulties identifying his own emotions, and social anhedonia. MVG's score on the EQ was 2.03 SD below the normal average. However, MVG's temporal experience of pleasure was in the normal range and there was no anosognosia (Table 3).

3.3. Complementary evaluations

We conducted an extended interview with MVG's wife, LG, to obtain more information about his behavioral changes after his stroke. LG stated that MVG had significant mood swings, with phases during which he would be very restless, or even impulsive, and phases during which he "was not doing well". LG also noticed other behavioral changes since the stroke. For example, MVG became more aggressive, especially verbally, but there was never any physical violence towards his wife or daughters. He also developed paranoid behavior, in that he had the impression that others "stared at him" and judged him negatively while, objectively, during situations in which she was present, no one paid attention to him. Moreover, he had become ironic and sarcastic, traits he never had before his stroke. Emotionally and relationally, LG described further modifications. MVG was more emotional (i.e., he cried while watching a "schmaltzy" movie). In contrast, he became indifferent to the feelings of his wife and daughters and he no longer expressed his own feelings.

LG also completed the *Iowa Rating Scales of Personality Change* to quantify and assess more precisely the sphere and amplitude of MVG's behavioral modifications. His total score, which was 80 points before the stroke, increased to 128 points after the stroke. A qualitative analysis of the answers suggested greater irritability, lack of initiative, a pessimistic mood, a slight decrease of persistence, reduced stamina, difficulties in planning, slight judgment difficulties, discrete anxiety, an increase in type A behavior (i.e., stress, restlessness), greater social withdrawal and much greater suspiciousness. The spheres in which the greatest personality changes were observed were

Table 2 e Performance of controls and MVG on the Faux-Pas Test, the First- and Second-order False-Belief Tasks, the RME Test and the Social Situations Test.

		MVG	Control group
Faux-Pas Test	Stories with Faux-Pas e Faux-Pas questions	32 ^a	52.83 (2.79)
	Stories with Faux-Pas e control questions	20	20 (0)
	Stories without Faux-Pas e Faux-Pas questions	20	19.83 (.57)
	Stories without Faux-Pas e control questions	20	20 (0)
False-Belief Task	ToM e 1st order	7	7.72 (1.08)
	ToM e 2nd order	5	5.4 (.69)
RME Test	Total score	16 ^a	25.91 (1.67)
Social Situations Test	Total score	32	35.15 (1.77)
	Appropriate	15	16.92 (1.61)
	Inappropriate	17	18.23 (1.17)
Maximum total scores, 60 for the Faux-Pas questions in stories containing a faux pas and 20 for other types of questions in the Faux-Pas Test, maximum total scores, 11 for the first order and eight for the second order false beliefs, maximum total score, 36 for the RME Test, and maximum total scores, 19 for appropriate as well as for the inappropriate situations.			
^a $p < .01$ compared with the control group.			

Percentage of MVG's and control group's correct answers on the questions relative to the faux-pas in stories containing a faux-pas

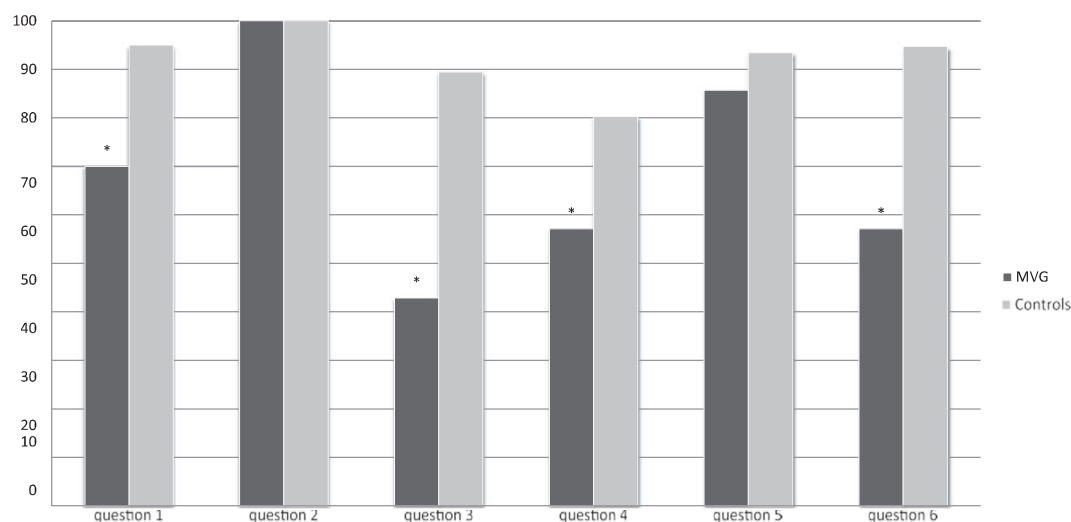


Fig. 2 e Detailed analysis of MVG's and controls' answers on the Faux-Pas Test. *MVG's score was significantly lower ($p < .01$) than that of the control group.

mood ("depression"), insensitivity, impatience, blunted affect/unemotional, apathy, inappropriate affect/emotion and vulnerability to pressure. In contrast, no changes were observed in the following domains: perseveration, impulsivity, obsessiveness (work), inflexibility, social inappropriateness, dependency, aggression, indecisiveness, vanity, frugality, manipulativeness and insight.

Finally, MVG underwent a *psychiatric consultation* to rule out any psychiatric origin of his observed disorders. Indeed, no patent clinical signs were observed, as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM), APA or the Classification Internationale des Maladies (CIM).

Table 3 e MVG's scores and normative data/interpretation of these scores for the different scales and questionnaires.

		MVG	Normative data/interpretation
STAI	State-anxiety	32	"High anxiety"
	Trait-anxiety	46	"High anxiety"
BDI		12	"Moderate depression"
TAS-20	Total score	67 ^a	44.52 (10.41)
	Identification	27 ^a	14.70 (5.36)
	Description	18	13.52 (4.29)
	Externalization	22	16.30 (4.23)
SAS		25 ^a	12.23 (5.21)
EQ		19 ^a	41.8 (11.2)
TEPS	TEPS e Total	4.4	4.23 (0.72)
	Consummatory	4.25	4.21 (.79)
	Anticipatory	4.33	4.22 (.63)
PCRS	MVG	97	
	Wife	101	
	Difference	-4	No anosognosia
	MVG e wife		

a Scores at 1.65 SD.

Although MVG experienced occasional sadness, he has not shown any evidence of mood disorders or psychotic symptoms (e.g., hallucinations, delirium, and dissonance). The consulting psychiatrist concluded that MVG's behavioral or emotional disorder was not linked to a personality disorder and there was no "pathological construction" of his personality. Moreover, there was no patent psychiatric antecedent.

3.4. Single photon emission computed tomography (SPECT)

A perfusion SPECT at rest was realized. The perfusion SPECT showed hypo-perfusion in the area of the left CN as in the left thalamus, in the right prefrontal and OF areas (Fig. 3).

4. Discussion

The aim of this study was to objectify the link between the BG and social cognition. We therefore performed a detailed evaluation of these abilities in a selected patient with a focal CN lesion. Whereas previous studies have highlighted the involvement of the frontal lobes in ToM and empathy (Baron-Cohen et al., 1994; Goel et al., 1995; Stone et al., 1998; Vollm et al., 2006), few studies have focused on the involvement of the sub-cortical structures in these abilities.

We found that, following a stroke in the territory of the left CN, our patient had difficulties of ToM in both verbal and visual modalities. It appears that his sequential organizational abilities and comprehension of a story (as assessed by the WAIS-III sub-test "picture arrangement") were intact, and memory deficits were thwarted by exposing the subject to the stories during the test. Thus, MVG's significantly lower scores, compared with control subjects, on the Faux-Pas Test were not due to a lower-level cognitive deficit. MVG's performance

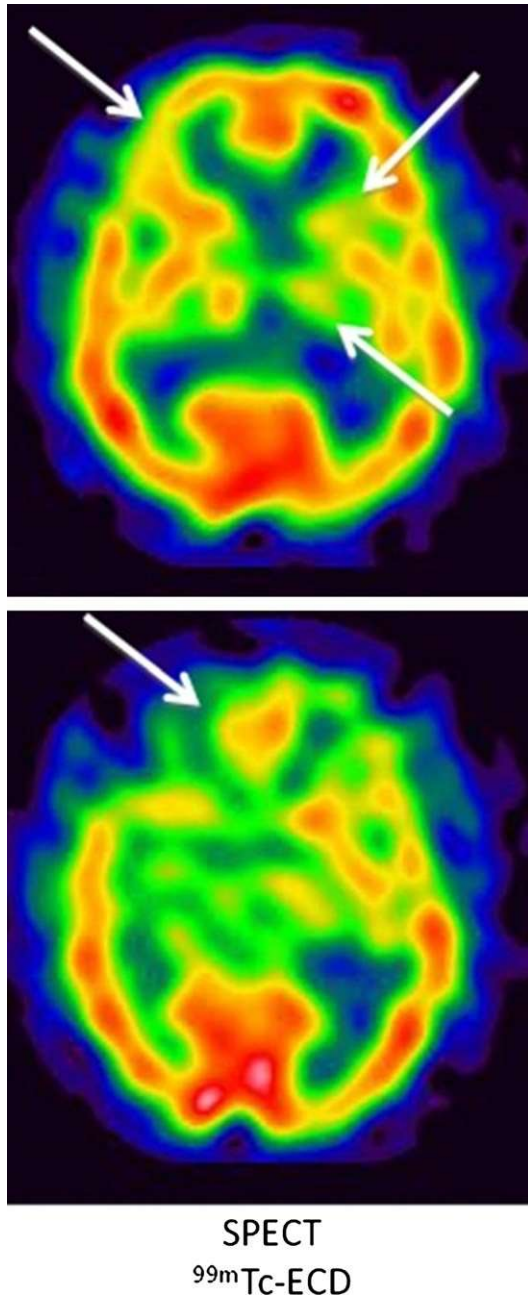


Fig. 3 e Transverse perfusion SPECT (99mTc-ECD): the SPECT images demonstrated decrease perfusion of left CN (lesional), as well as the left thalamus, the right prefrontal and right OFC (functional diaschisis) (white arrows).

on the First- and Second-order False-Belief Tasks, however, were similar to those of the control group, indicating that the “warm” or “affective” part, not the “cold” or “cognitive” part, of ToM was altered by the stroke.

Furthermore, the RME Test objectified MVG’s major difficulties in inferring subtle mental states based on viewing pictures of someone’s eyes. Since his Eye Direction Detector (EDD), (Baron-Cohen, 1995), a precursor module of the ToM, was intact, as shown by the Mutual Gaze Detection Test, MVG’s significantly lower score, in comparison with the control group,

on the RME Test is indicative of his visual ToM impairment. This is also important for understanding of some behavioral changes in MVG, including the emergence his “paranoid” behavior (e.g., he constantly thinks that people are staring at him and judge him negatively) since his stroke, in the sense that they are not due to an alteration in gaze processing.

Another disorder in which behavioral and emotional disorders have been reported is “acquired sociopathy” (Damasio, 1994), indicative of many disorders that affect the more precise recognition of facial expressions, emotional reactions and social cognition. These patients’ behavior may therefore be a consequence of damage to the OF loop implicated in ToM (Baron-Cohen, 1995). Hence, patients who have difficulties inferring others’ mental states may also have problems in modulating their own emotional and social behavior. Since MVG shows such behavioral modification and ToM deficits since his stroke, these aspects deserve further assessment. However, MVG’s performances on the Moral and Conventional Judgments Task and the Social Situations Test showed that his comprehension of moral and conventional social rules and formal social bans or permissibilities were preserved after damage to his left CN.

Our results thus indicate that impairment to ToM is not necessarily accompanied by a total loss of knowledge related to moral and conventional rules and appropriate behavior, similar to that observed in acquired sociopathy. This leads us to hypothesize the existence of two distinct and independent systems, a hypothesis supported by the results of a patient (JS) who showed a profile opposite to that of MVG (Blair and Cipolotti, 2000). Since an injury to his frontal lobes, JS has suffered from acquired sociopathy; although he showed major difficulties in the two tests mentioned above, his ToM was preserved.

Furthermore, we found that MVG had difficulties on the Ekman and Friesen Emotion Recognition Test, especially in recognizing facial expressions of fear and sadness. Since he performed normally on Benton’s Facial Recognition Test (Benton and Van Allen, 1968), the observed deficit on the former test was likely not due to a deficient perception of faces. The results on this test further enabled us to draw a parallel with more qualitative data, by objectifying empirically the very precise complaint expressed by MVG, that is, a loss of the ability to recognize negative emotions in others.

Other parallels between MVG’s results on social cognition questionnaires and the findings from more qualitative evaluations can be made. For example, the EQ was used to assess MVG’s empathy abilities by means of a self-reported questionnaire. We note that the score obtained by MVG is close to that of people with high functioning autism and people with Asperger’s syndrome (Baron-Cohen and Wheelwright, 2004). It is indeed much lower than healthy men’s and reflects clearly a disturbance of empathy, which objectifies the loss of empathy in MVG, as described by himself and his wife (e.g., he became insensitive to his daughters’ crying). Similarly, MVG’s EQ score, as well as his poor performance on the last question in the Faux-Pas Test (i.e., “How do you think Y felt?”), requiring some empathic understanding of how the person in the story would feel, can be compared to important modifications in some of the spheres addressed by the Iowa Rating Scales of Personality Change, highlighting, among others,

increased insensitivity, blunted affect and more inappropriate affect and emotion.

Thus, our findings in MVG indicate that localization of focal damage to the area in the dorso-medial part of the head of the left CN can lead to ToM disorders. Among these are a disruption in the “affective” part of ToM, difficulties in inferring mental states by viewing pictures of someone else’s eyes and an impairment of emotion recognition. These observations tended to confirm our first hypothesis.

We also formulated a second hypothesis that a disconnection in the sub-cortical OF circuit resulting from a lesion of a BG may be the origin of the disturbances in the domain of social cognition. Damage to the frontal cortex, especially to the OFC, can lead to disturbances in social cognition. Following OF lesions, patients often show impaired performances on the Faux-Pas Test, coupled with relatively correct performances on First- and Second-Order False-Belief Tasks (Shamay-Tsoory and Aharon-Peretz, 2007), in agreement with the hypothesis that the OFC is involved in the “warm” aspects of ToM (Brothers and Ring, 1992). Moreover, this area is involved in the recognition of emotions (Hornak et al., 1996) and interpreting others’ mental states from their eyes (Sabbagh et al., 2004). Many patients with lesions in this area show severe impairment of their social functioning (Blumer and Benson, 1975; Saver and Damasio, 1991). Theoretically, these patients may be able to analyze social situations correctly, but they may behave inappropriately in real life. Other consequences commonly observed include impulsive reactions, difficulties in tolerating frustration (Burgess and Wood, 1990) and sporadic aggression, more often directed towards objects than other people. The OFC is regarded as crucial in these emotional and behavioral modifications (Damasio, 1994; Grafman et al., 1996; Volavka, 1995). The way these individuals experience emotions may be decreased or amplified; moreover, they may be indifferent to suffering caused by their behavior (Ollat and Pirot, 2004). Thus, they have difficulties involving different aspects of social cognition, together with the relative preservation of their intellectual abilities (Damasio et al., 1991). In sum, we found that the performance of MVG on these tasks, as well as his behavioral changes observed in everyday life, were parallel to that observed for OFC patients. Similarly, MVG’s symptom pattern can be related to that of patients suffering from the frontal variant of frontotemporal lobar degeneration, in which the impaired cerebral regions [i.e., mesial frontal, OF, and anterior insular cortices (Davatzikos et al., 2008; Hornberger et al., 2011; Seeley et al., 2008)] have been implicated in social cognition processes. These patients show also specific impairments of social cognition, including ToM [e.g., (Gregory et al., 2002; Modinos et al., 2009; Snowden et al., 2003)], emotion recognition [e.g., (Lough et al., 2006; Snowden et al., 2008)] and empathy [e.g., (Eslinger et al., 2011; Fernandez-Duque et al., 2010)].

The SPECT findings of MVG showed hypo-perfusion in the territory of his left CN, as well as a discrete right prefrontal (more precisely in the inferior area) and right OF hypo-perfusion. Indeed, the mPFC, especially Brodmann Areas 8 and 9, is crucial in social cognition, as shown by functional neuro-imaging studies in healthy adults (Fletcher et al., 1995; Russell and Sharma, 2003). These areas are activated while

participants are inferring mental states about others’ beliefs and deceptions. Similarly the ventro-medial PFC was shown to be activated when individuals were asked to attribute mental states to themselves and others (Lombardo et al., 2010). The OFC is particularly important in ToM, since this specific area is activated during recognition of mental state terms (Baron-Cohen et al., 1994). Studies using event related potentials also confirmed the involvement of the medial PFC in ToM activities (Sabbagh and Taylor, 2000), providing further evidence that the PFC, especially the OFC, plays a key role in social cognition.

Nevertheless, hypo-perfusion in the prefrontal (i.e., ventro-medial) areas was unexpected, given the model of the frontal sub-cortical loops. Two of these five parallel and segregated loops involve the CN: the DL circuit, involving the DL part of the head of the caudate; and the OF loop, comprising the ventro-medial part and extending from the head to the tail of this structure (Alexander et al., 1986). Although the OF loop is involved in social and emotional functioning, while the DL circuit is involved in regulating executive functions, there is evidence in animal studies for interactions between the main projection lines, both within the BG and between external structures (Groenewegen et al., 1999; Haber, 2003; Joel and Weiner, 1994). Moreover, the word “circuit” does not imply a rigidly self-enclosed pathway without substantial inputs and outputs to other structures (Alexander et al., 1986). These findings may explain MVG’s cognitive profile. Indeed, MVG experienced damage to the dorso-medial part of the head of the left CN, which is regarded as crucial for executive functioning, but less so for social cognition. However, the opposite was observed in our patient; that is, his ToM and emotion recognition abilities (i.e., social cognition) were impaired while his executive functions were preserved. Although these findings may be due to interconnections among the various loops, sub-divisions within the caudate, relative to belonging to different loops, may be less precise than described [i.e., the ventro-medial part belong to the OF loop and DL part belonging to the DL circuit (Tekin and Cummings, 2002)]. Moreover, damage to MVG’s caudate was not confined to either the ventro-medial or DL part of the structure, but extended slightly over the two areas (i.e., the “dorso-medial” part of the caudate). Thus, the anatomo-functional organization of the frontal sub-cortical circuits may not be as segregated and parallel as stated by previous studies. Furthermore, one could wonder about the more pronounced hypo-perfusion in the right OF area, whereas the initial damage is located in the left CN. This result could be explained by the fact that the connections between the BG and the cortex may not exclusively be ipsilateral. Indeed, crossed projections between the frontal lobes and the caudate nuclei have been shown in the rhesus monkey (Fallon and Ziegler, 1979).

In conclusion, we have provided a detailed description of a patient with selective impairment of social cognition abilities following focal damage to his left CN. The results of our evaluations, the symptoms displayed by MVG, the description of his symptoms by his family and friends, and imaging outcomes seem to confirm our hypothesis, that impairment of one of the BG pertaining to one of the circuits induces deficits similar to those induced by a lesion in the cortical area belonging to that loop. Consequently, these findings favor the

frontal sub-cortical model and suggest the necessity of the integrity of the entire fronto-sub-cortical circuit so that the different functions (subtended by the structures belonging to it), can work out properly. Indeed, MVG's deficits suggest a disturbance in the connectivity among cortico-sub-cortical networks due to damage to the head of the left CN, with this disconnection selectively involving the OF loop.

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