

Correspondence

Psychological Medicine, 48 (2018).

doi:10.1017/S0033291717002252

First published online 24 August 2017

Research Letter

Auto-activation deficit in schizophrenia: a case report

Apathy is conventionally defined as the quantitative reduction of self-generated voluntary and purposeful behaviors (Levy & Dubois, 2006). Interestingly, ‘auto-activation’ deficit (AAD), the most severe form of apathy, has been previously described to be secondary to bilateral, restricted and specific lesions in the pallidum, striatum and thalamus (Levy & Dubois, 2006). Here we report the case of a patient with schizophrenia who had AAD and was treated with pramipexole, a dopamine agonist.

Mr M. is a 38-year-old unemployed right-handed single man who fulfilled the DSM-5 diagnostic criteria for schizophrenia and who presented with severe apathy. His first psychiatric hospitalization occurred in 2013 following admission to an emergency service after ingesting a ‘dead duck’ found on the floor. He then presented resuscitated cardiorespiratory arrest (10 min of no-flow) revealing idiopathic chronic heart failure. Following this episode, he presented quasi-mutism, with hermetic speech, persecutory delusion and auditory hallucinations. Additionally, he experienced anterograde and retrograde memory loss. There was no history of seizure, neurological disease or other significant major medical condition. A family history of schizophrenia was also found in one of his second-degree relatives. Mr M. was admitted to our Psychiatry Department in April 2016 for resistant and severe apathy. Mr M. needed external solicitation for his daily activities, such as eating or washing himself (e.g. he almost got burned by staying too long in his shower until he was told to turn the water off). Replies to questions were laconic and frequently incomplete. We also noted an important anosognosia. All examinations performed to explore the different potential causes of his apathy were normal.

Structural brain MRIs were performed in 2013 and 2016 and were normal. A (18F)-Fluorodesoxyglucose Positron Emission Tomography (FDG-PET) brain scan was performed in April 2016 and revealed bithalamic hypometabolism particularly marked on the

antero-medial right side and bifrontal hypometabolism (Fig. 1), probably linked to his resuscitated cardiorespiratory arrest. Comparison with an age-matched normal subject database (Scenium VD 20, Siemens) confirmed the bithalamic hypometabolism (-6.2 and -5.8 standard deviations (s.d.)). We made the diagnosis of AAD. The severity of schizophrenia and AAD were also assessed using PANSS (total=98, Positive=14, Negative=40, General=44) and the Lille apathy rating scale (LARS) (Sockeel *et al.* 2006). The LARS caregivers’ version was 27/36 (severe apathy).

Mr M. was initially treated with long-acting injectable antipsychotic (risperidone 37.5 mg/14 days). We first switched to risperidone 3 mg per os/day (first FDG-PET brain scan) and then decided to add pramipexole (a dopaminergic agonist) to treat apathy, as it has shown relative safety in schizophrenia (Kelleher *et al.* 2012). Pramipexole was prescribed three times a day and gradually increased to 5 mg/day. After 2 months of treatment, we decided to gradually withdraw risperidone, as the treatment response was too low. His parents reported a clinical improvement after he had taken pramipexole for 2 months (LARS caregivers’ version = 22/36, -19%). Four months after he stopped risperidone, this improvement was more marked (LARS caregivers’ version = 11/36, -59%). The positive symptoms of schizophrenia were slightly increased (vague delusion that does not interfere with behavior), but the overall score was stable (Positive = 18, Negative = 34, General = 45, Total = 97). No other adverse effects were noted. A PET scan was performed 4 months after risperidone was interrupted, which confirmed the functional improvement in frontal and thalamic neurometabolism (-5.1 and -4.3 s.d.) (Fig. 1). We showed an association between an increasing dose of the dopamine D3 agonist (i.e. pramipexole), a decreasing dose of the dopamine D2–D3 antagonist (risperidone), and the clinical improvement as assessed by the LARS and the restoration of the thalamic metabolism as seen in the PET scan evolution.

In this case, we showed a strong correlation between an increasing dose of the dopamine agonist (i.e. pramipexole), the clinical improvement as assessed by the LARS and the restoration of the thalamic metabolism as seen in the PET scan evolution. Even if we are unable to ascertain that these changes are specific to pramipexole alone, we believe that the dopamine balance was probably improved between: (i) the decreased dopaminergic transmission associated with AAD (Chong & Husain, 2016) and (ii) the mesolimbic

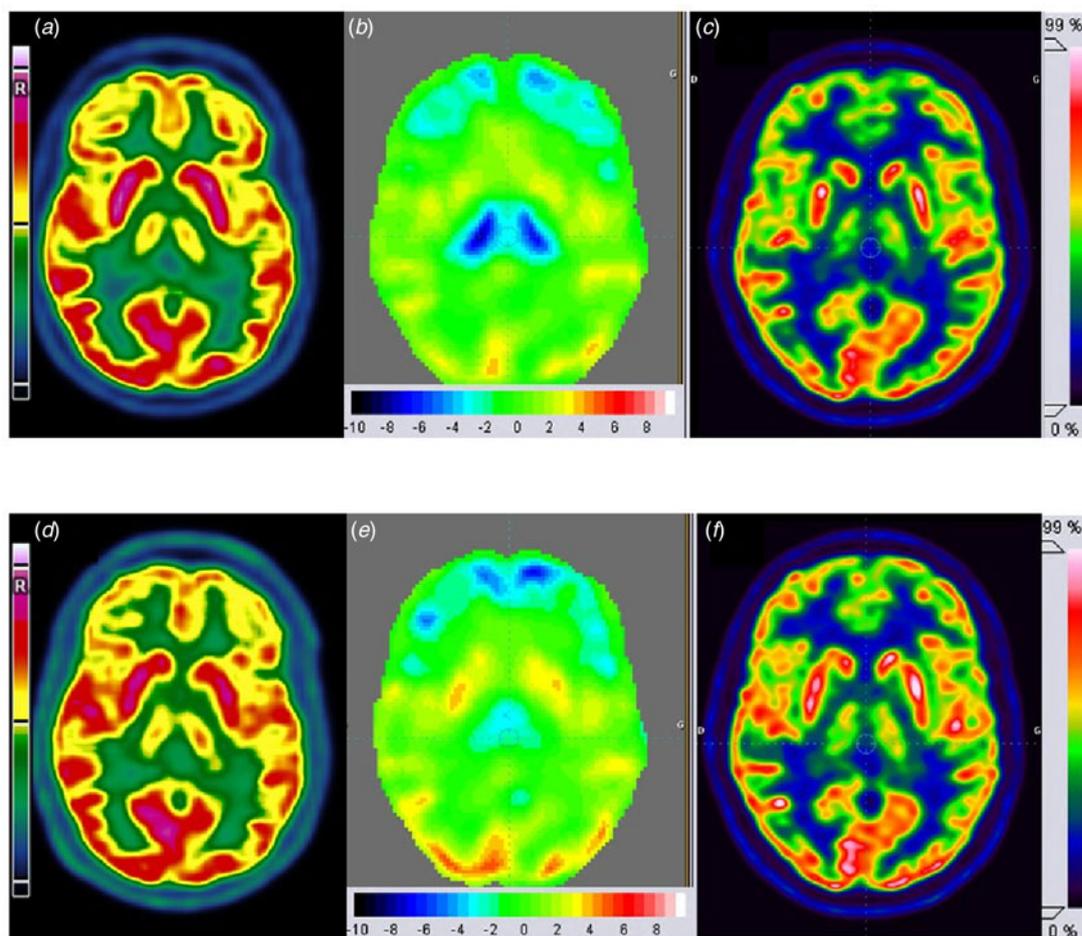


Fig. 1. Positron Emission Tomography (FDG-PET) brain scan obtained 30 min after injection of 185 MBq of (18F)-Fluorodesoxyglucose on Biograph mCT 16 (Siemens MS, Knoxville, USA) before (*a–c*) and after (*d–f*) treatment. (*a, d*) Conventional FDG-PET transverse reconstructions showing decreased uptake in thalamic regions and frontal hypometabolism. (*b, e*) Database comparison results in standard deviation of the mean with a significant decrease in metabolism shown in blue (Scenium VD20) and (*c, f*) corresponding reoriented, normalized high definition FDG-PET slices after alignment to the database template.

hyperdopaminergia associated with schizophrenia. Interestingly, functional imaging, such as PET, appears to be a useful tool that is probably underused in complex neuropsychiatric cases (Amen *et al.* 2011).

Acknowledgements

The authors wish to thank Dr Emilie Mautret for her help in the management of the patient.

Consent for publication

Written informed consent was obtained from the patient's parents for publication of this case report and any accompanying images.

Declaration of Interest

None.

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A. LEROY^{1,*}, G. PETYT², B. PIGNON^{3,4,5,6}, G. VAIVA¹,
R. JARDRI¹ AND A. AMAD^{1,7}

¹Univ. Lille, CNRS, UMR 9193-PsyCHIC-SCALab & CHU Lille,
Department of Psychiatry, Lille, France

²Nuclear Medicine Department, CHU Lille, PET Center R. Salengro,
Lille Cedex, France

³AP-HP, DHU PePSY, Hôpitaux universitaires Henri-Mondor, Pôle
de Psychiatrie, Créteil, France

⁴INSERM, U955, team 15, Créteil, France

⁵Fondation FondaMental, Créteil, France

⁶UPEC, Université Paris-Est, Faculté de médecine, Créteil, France

⁷Department of Neuroimaging, Institute of Psychiatry, Psychology
and Neuroscience, King's College London, London, UK

*Address for correspondence: A. Leroy, Hôpital Fontan,
CHRU de Lille, Lille cedex F-59037, France.
(Email: arnaud.g.leroy@wanadoo.fr)