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Disappearance of Henry Maudsley

In 1991, I published a paper entitled 'Whatever happened to Henry Maudsley?',[1] in which I had deduced that the most likely reason for his sudden and inexplicable disappearance was the onset of an attack of clinical depression.

I further deduced that his malady was primarily precipitated by the death of his wife, although secondary factors were at work of which there are two main ones. The first was that his was a childless marriage so that the loss of his wife resulted in the loss of his only emotional prop; second, his father had behaved in an identical way when his wife, Maudsley's mother, had died.

It was only after the publication of my paper that I realised that my explanation, although certainly feasible, was based on mainly circumstantial evidence, so that, instead of solving the enigma of Maudsley's disappearance, I had complicated it. But it was too late; I had no option but to rest my case. And this is how the position would be today if serendipity had not taken a hand in the game.

It happened that while researching material about the Victorian alienists, I came across a paper, previously unknown to me, by Dr Thomas Walmsley concerning Sir James Crichton-Browne, probably the doyen of psychiatrists at that time.

Dr Walmsley refers in this paper to the occasion when Sir James delivered the first Maudsley lecture to the Royal Medico-Psychological Association in 1920. It is in this paper that Sir James 'recalled the optimistic and energetic Henry Maudsley with whom he had been friendly in the 1860s. With some feeling [the use of this expression is important in that any demonstration of emotion in public at that time would have been considered infra dig], he contrasted the morose and reclusive Maudsley of later years.'[2]

I remember that at this point I emitted a whoop, a mélange of joy and relief – my supposition as to the disappearance of Henry Maudsley had been vindicated!

1 Rollin H. Whatever happened to Henry Maudsley? In *150 Years of British Psychiatry, 1841–1991* (eds GE Berrios, H Freeman): 351–8. Gaskell, 1991.

2 Walmsley T. Crichton-Browne's biological psychiatry. *Psychiatr Bull* 2003; **27**: 20–2.

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Serotonin and the mode of action of electroconvulsive therapy

The French philosopher Pierre Charron wrote that the true science and study of man is man. Professor Yatham and colleagues deserve commendation for their application of modern brain imaging techniques to study the mode of action of electroconvulsive therapy (ECT) in living patients with depression.[1] The final assertion that their findings may put to rest the controversy about the role of brain serotonin in mediating the antidepressant effects of ECT may, however, be premature.

The authors suggested a common mode of action among ECT and antidepressant drugs, that is, the down-regulation of brain 5-HT_2 receptors. There is, however, evidence to question the overlap between the mode of action of ECT and antidepressant drugs that target serotonin. Selective serotonin reuptake inhibitors (SSRIs) inhibit the serotonin transporter. The gene that encodes the serotonin transporter has a promoter region that contains a polymorphism, and the allelic status of this polymorphism is associated with the probability of both improvement and recovery with an SSRI. The allelic status of this polymorphism is not associated with the outcome of ECT.[2] A proportion of patients with depression treated successfully with an SSRI will experience transient relapse during acute tryptophan depletion, which in turn depletes serotonin. This is not observed in patients with depression treated successfully with ECT.[3]

There is also evidence to suggest more of an overlap between the mode of action of ECT and antidepressant drugs that target catecholamines. A history of failure to recover with an SSRI during the index episode has no bearing on the probability of remission from unipolar non-psychotic major depression with subsequent ECT; in contradistinction, such a failure with bupropion, which does not target serotonin at all, or a heterocyclic antidepressant is associated with a reduced probability of remission with subsequent ECT. The only known allelic status that is associated with the outcome of ECT in patients with depression concern polymorphisms believed to affect the concentration of dopamine in the forebrain.[4] Modern brain imaging techniques have also been applied to study the effects of ECT on brain dopamine: binding to the D_2 receptor in the rostral anterior cingulate, an area of the brain implicated in the pathophysiology of depressive illness, fell by 25% over a course of bilateral ECT, a finding compatible with an increase in the availability of dopamine.[5]

None of these observations on its own disproves the hypothesis suggested by the authors. Nevertheless, these observations too concern living patients with depression treated by ECT, and together cast doubt on the central role of brain serotonin in the mode of action of ECT in major depression.

1 Yatham LN, Liddle PF, Lam RW, Zis AP, Stoessl AJ, Sossi V, et al. Effect of electroconvulsive therapy on brain 5-HT_2 receptors in major depression. *Br J Psychiatry* 2010; **196**: 474–9.

2 Rasmussen KG, Black JL. Serotonin transporter gene status and electroconvulsive therapy outcomes: a retrospective analysis of 83 patients. *J Clin Psychiatry* 2009; **70**: 92–4.

3 Cassidy F, Murry E, Weiner RD, Carroll BJ. Lack of relapse with tryptophan depletion after successful treatment with ECT. *Am J Psychiatry* 1997; **154**: 1151–2.

4 Domschke K, Zavorotnyy M, Diemer J, Nitsche S, Hohoff C, Baune BT, et al. COMT val 158met influence on electroconvulsive therapy response in major depression. *Am J Med Genet Part B* 2009; **153B**: 286–90.

5 Saijo T, Takano A, Suhara T, Arakawa R, Okumura M, Ichimiya T, et al. Electroconvulsive therapy decreases dopamine D_2 receptor binding in the anterior cingulate in patients with depression: a controlled study using

positron emission tomography with radio ligand [11c] FLB 457. *J Clin Psychiatry* 2010; **71**: 793–9.

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A care pathway for schizophrenia

Swaran Singh has recently argued for a care pathway for psychosis or schizophrenia.[1] We have recently argued for a staging approach to schizophrenia.[2] Such an approach argues that there are different stages in the development of schizophrenia, and that therefore different stages of the illness will require different interventions to optimise treatment, be it pharmaceutical, social or psychological. Furthermore, logically, the different stages will require different goals of treatment and different expected outcome measures. Thus, for example, the aim of treatment in the first or 'at risk mental state' stage of psychosis is to prevent psychosis developing, while the aim of the second stage, or the first-episode stage, is to end the psychotic episode and return the patient to work and education.

Staging in schizophrenia also extends to the phase of chronic illness, and here the goal will be, depending on the severity of the illness, to limit the positive and negative symptoms of the illness, to prevent relapse, and to optimise social inclusion, promoting a return to work if possible. Such a staging approach to schizophrenia is underpinned by the neuroimaging evidence, since the loss of grey matter linked with schizophrenia does start in the prodromal 'at risk' phase, becomes more prominent in the first episode, and then becomes incrementally more severe in the later stages of the disease.[3–5] Furthermore, different stages of the illness appear to be mirrored in different patterns of change in such structures as the hippocampus and the amygdala,[6] as well as changes in pituitary volume.[7,8] Thus, a 'staging approach' to schizophrenia does provide a logical framework for the development of a care pathway for schizophrenia, with different stages or phases requiring the development of specialised teams with different expected outcomes, but who will always, in each phase of the illness, strive to optimise treatment in order to achieve the best results. Hence, such a pathway may include an 'at risk mental health' team, which will attempt to reduce the rate of transition to full psychosis in patients who are developing 'prodromal' symptoms. This would be followed in the pathway by a first-episode service which will work assertively with patients so as to deal with the first episode and return patients to work and education, and at the other end of the spectrum, assertive outreach teams will work with patients who are difficult to treat who have demonstrated the most serious deterioration in functioning.

What, however, is missing in this care pathway is the treatment of those patients who are returned to community mental health teams (CMHTs) after 3 years in an early intervention service and who are not deemed ill enough to require referral to the assertive outreach teams. These constitute the majority of patients with long-term schizophrenia. Unfortunately, since CMHTs have other priorities, and indeed are oriented to dealing with patients with relatively less severe forms of mental illness, many of these patients may receive suboptimal care, sometimes consisting of the simple delivery of medication within a depot or clozapine clinic, and without the systematic delivery of psychosocial interventions. As a result, in many cases, social inclusion is not optimised as a direct result of the loss of the assertive approach to care. It is therefore small wonder that both the Lambeth Early Onset (LEO)[9] and the OPUS[10] services report a loss of improvement in outcomes within 5 years of first treatment, after patients have been transferred from early intervention teams to the care of CMHTs.

It is of interest that a study in Russia,[11] where patients were followed up assertively for 5 years, has shown no such loss of improvement in outcomes. It is urgent that the development of ongoing assertive, specialised teams for psychosis, as suggested by Singh, should proceed in order to complete the schizophrenia care pathway. The CMHT cannot provide such an assertive service, since it is focused on other things. Seen in this perspective, recent suggestions that early intervention and assertive outreach teams should be amalgamated into CMHTs and provide elements of specialised care within the CMHTs must further confuse the focus of the CMHTs and constitute a serious misreading of the evidence.

1 Singh SP. Early intervention in psychosis. *Br J Psychiatry* 2010; **196**: 343–5.

2 Agius M, Goh C, Ulhaq S, McGorry P. The staging model in schizophrenia, and its clinical implications. *Psychiatr Danub* 2010; **22**: 211–20.

3 Meisenzahl EM, Koutsouleris N, Gaser C, Bottlender R, Schmitt GJ, McGuire P, et al. Structural brain alterations in subjects at high-risk of psychosis: a voxel-based morphometric study. *Schizophr Res* 2008; **102**: 150–62.

4 Meisenzahl EM, Koutsouleris N, Bottlender R, Scheuerecker J, Jäger M, Teipel SJ, et al. Structural brain alterations at different stages of schizophrenia: a voxel-based morphometric study. *Schizophr Res* 2008; **104**: 44–60.

5 Pantelis C, Yücel M, Wood SJ, Velakoulis D, Sun D, Berger G, et al. Structural brain imaging evidence for multiple pathological processes at different stages of brain development in schizophrenia. *Schizophr Bull* 2005; **31**: 672–96.

6 Velakoulis D, Wood SJ, Wong MT, McGorry PD, Yung A, Phillips L, et al. Hippocampal and amygdala volumes according to psychosis stage and diagnosis: a magnetic resonance imaging study of chronic schizophrenia, first episode psychosis, and ultra-high-risk individuals. *Arch Gen Psychiatry* 2006; **63**: 139–49.

7 Pariante CM, Vassilopoulou K, Velakoulis D, Phillips L, Soulsby B, Wood SJ, et al. Pituitary volume in psychosis. *Br J Psychiatry* 2004; **185**: 5–10.

8 Garner B, Pariante CM, Wood SJ, Velakoulis D, Phillips L, Soulsby B, et al. Pituitary volume predicts future transition to psychosis in individuals at ultra-high risk of developing psychosis. *Biol Psychiatry* 2005; **58**: 417–23.

9 Gafoor R, Nitsch D, McCrone P, Craig TKJ, Garety PA, Power P, et al. Effect of early intervention on 5-year outcome in non-affective psychosis. *Br J Psychiatry* 2010; **196**: 372–6.

10 Bertelsen M, Jeppesen P, Petersen L, Thorup A, Øhlenschlæger J, le Quach P, et al. Five-year follow-up of a randomized multicenter trial of intensive early intervention vs standard treatment for patients with a first episode of psychotic illness. *Arch Gen Psychiatry* 2008; **65**: 762–71.

11 Zaytseva Y. Efficacy of integrated program treatment of first episode patients versus standard care. *Psychiatr Health* 2008; **10**: 51–7.

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Author's reply: I am grateful for Dr Agius' comments and entirely agree that a staging approach allows the development of a comprehensive care pathway for psychotic disorders. With such an approach, the most efficacious and potentially less harmful interventions can be appropriately targeted at an earlier clinical stage of an emerging illness. Such a staging model is widely used in medicine and has recently been described as a heuristic framework for intervening early in all youth mental health problems.[1,2]

Half of all adult mental disorders begin in late adolescence, usually with an initial presentation of non-diagnostic symptoms. Mental health services, especially community mental health teams (CMHTs), offer interventions only when an illness is severe