original papers

References

ALLEN, D. (1999) Mediator analysis: an overview of recent research on carers supporting people with intellectual disability and challenging behaviour. *Journal of Intellectual Disability Research*, **43**, 325–339.

DEPARTMENT OF HEALTH (2001) *Valuing People: A New Strategy for Learning Disability for the 21st Century.* TSO (The Stationery Office).

DEPARTMENT OF HEALTH (2004) *Green Light for Mental Health: How Good Are Your Services for People with Learning Disabilities? A Service Improvement Toolkit*. http://www.valuingpeople.gov.uk/documents/MentalHealthGLGuide.pdf.

GRALTON, E., PEARSON, S., SUTHERLAND, A., *et al* (2001) The environment psychiatric patients create for themselves. The varying perceptions of professional staff. *Psychiatric Bulletin*, **25**, 134–137.

HALL, I., PARKES, C., HIGGINS, A., *et al* (2006) The development of a new integrated mental health service for people with learning disabilities. *British Journal of Learning Disabilities*, **34**, 82–87.

HERVEY, N. & RAMSAY, R. (2004) Carers as partners in care. *Advances in Psychiatric Treatment*, **10**, 81–84.

LACEY, Y. & THOMAS, P. (2001) A survey of psychiatrists' and nurses' views of mental health advocacy. *Psychiatric Bulletin*, **25**, 477–480.

MOSS, S., PATEL, P., PROSSER, H., *et al* (1993) Psychiatric morbidity in older people with moderate and severe learning disability. II. Development and reliability of the patient interview (PAS–ADD). *British Journal of Psychiatry*, **163**, 471–480.

ROSE, D. (2001) *Users' Voices. The Perspectives of Mental Health Service Users on Community and Hospital Care.* Sainsbury Centre for Mental Health.

SAINSBURY CENTRE FOR MENTAL HEALTH (1998) *Acute Problems: A Survey fo the Quality of Care in Acute Psychiatric Wards.* Sainsbury Centre for Mental Health.

Sarah Samuels Royal Free and University College Medical School, London, **Ian Hall** Islington Learning Disabilities Partnership, London, **Charles Parkes** Camden Learning Disabilities Service, London, ***Angela Hassiotis** Department of Mental Health Services, Royal Free and University College Medical School, 48 Riding House Street, London W1W 7EY, email: a.hassiotis@ucl.ac.uk

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MARC LYALL, ANGELA PRYOR AND KEVIN MURRAY

Clozapine and speech dysfluency: two case reports

AIMS AND METHOD

We describe two patients, both diagnosed with psychotic illnesses, who developed stuttering while being treated with clozapine.

RESULTS

In both patients the stuttering was severe and significantly impaired progress towards recovery. Deviant speech dimensions and voice quality were consistent with dysarthria and dystonia.

CLINICAL IMPLICATIONS

Patients who develop abnormal electroencephalogram activity and those who have a family or personal history of stuttering might be at increased risk of developing speech problems with clozapine. Speech dysfluency might be a consequence of clozapine's action in lowering the seizure threshold. Potential management strategies include the use of sodium valproate and changing the type of antipsychotic.

Stuttering is defined as a disturbance in the normal fluency and time patterning of speech, characterised by sound and syllable repetitions, sound prolongations and broken words (American Psychiatric Association, 1994). The prevalence of stuttering in the general population is slightly less than 1%, with a peak age at onset in early childhood (Craig *et al*, 2002). Causation remains uncertain, but many have argued that people who stutter have a subtle neurological dysfunction that disrupts the precise timing required to produce speech (Guitar, 1985). A family history of stuttering is evident in about 60% of people with an onset in childhood (Andrews *et al*, 1988).

A link between schizophrenia and stuttering is recognised and Rogers (1985) reported a 2% prevalence rate in patients with chronic schizophrenia. The relationship between stuttering and antipsychotic treatment is complex. There are a number of case reports of patients who have developed stuttering when prescribed phenothiazines (Nurnberg & Greenwald, 1981; Adler *et al*, 1987). Conversely, trifluoperazine and haloperidol have been shown to be effective treatments for the stuttering associated with schizophrenia (Menkes & Ungarvi, 1993).

There are no previous reports in the British medical literature of a link between clozapine and stuttering. However, four cases have been reported in North America. Two reports describe stuttering in young women prescribed clozapine, one at a dose of 125 mg, the other at 400 mg (Thomas *et al*, 1994; Ebeling *et al*, 1997). In two other patients the development of stuttering has been associated with seizure activity. Supprian *et al* (1994) described a 49-year-old woman who began to stutter when prescribed 700 mg clozapine. On 750 mg clozapine she suffered a generalised epileptic seizure accompanied by polyspike wave activity on an electroencephalogram (EEG). She was treated with sodium valproate; the stuttering remitted and did not recur when she was prescribed 600 mg clozapine daily. Duggal *et al* (2002) reported a 28-year-old man who developed stuttering on 300 mg clozapine daily. At 450 mg clozapine he suffered a generalised seizure. As the dose was reduced to 200 mg the stuttering stopped. Sodium valproate was later started.

In this paper, we describe two patients who developed stuttering while being treated with clozapine on the same ward in a high secure hospital.

Case reports

Patient 1

A 62-year-old man, a former market trader, was detained in hospital following an assault on his partner. He has no

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family history of speech dysfluency. He first displayed symptoms of psychosis at the age of 31. Over the course of several months he developed persecutory beliefs centring on the actions of his partner. He was admitted for a short period to a psychiatric hospital and treated with medication. The patient did not report speech dysfluency at this time.

His symptoms appear to have diminished and continued in remission for many years. In the late 1990s, however, the patient developed a belief that his partner was plotting to kill him. Over the course of a year the patient's mental state deteriorated further and he eventually attacked his partner.

Initially the patient was considered to have a personality disorder and received a lengthy prison sentence. However, his paranoia became increasingly evident and he was eventually transferred to hospital where a delusional disorder was diagnosed. He was initially treated with flupenthixol decanoate, but with limited effect. After 2 months of oral risperidone, clozapine was started.

Within a month of taking 50 mg clozapine daily, the patient's speech was noted to be abnormal. As the dose of clozapine was increased to 125 mg these difficulties became more prominent and the patient's speech became almost unintelligible. However, when the dose was subsequently reduced to 75 mg, giving a serum clozapine level of 0.09 mg/l (normal therapeutic range 0.35–0.42 mg/l; Taylor *et al*, 2005), there was some improvement.

A speech and language therapy assessment revealed a constant and severe orofacial dyskinesia, which had not been noted previously. The quality of the patient's voice was harsh and strangulated. He was unable to sustain phonation and his speech rate was characterised by irregular articulatory breakdown, hesitations and sound repetitions. The repetitions were not associated with any particular speech sound and occurred at irregular word positions throughout his speech utterances. The deviant speech dimensions and voice quality were consistent with slow hyperkinetic dysarthria and dystonia (Murdoch, 1990). An EEG was normal and the patient's stuttering was felt to likely result from clozapine-related tardive dystonia affecting the laryngeal and pharyngeal muscles.

Tetrabenazine was prescribed and the patient was then able to tolerate an increase in the dose of clozapine to 100 mg daily (serum level 0.09 mg/l). However, attempts to increase the dose of clozapine further resulted in unacceptable dysarthria, despite increases in tetrabenazine dosage. Eventually clozapine was withdrawn. The patient's speech pattern returned to normal. After a washout period, quetiapine was started. This did not cause any side-effects, but made little difference to the patient's mental state.

Patient 2

A 55-year-old man was convicted of a violent attack on a friend. The patient's father and paternal uncle had a pronounced stammer, and the patient's brother has a mild stammer. The patient denies any personal history of speech dysfluency. He appears to have developed paranoid schizophrenia in his early 20s.

In 1993 the patient suffered a head injury. Subsequent neuropsychological testing revealed problems with executive functioning and a significant discrepancy between the patient's verbal and performance IQ, which was felt to be related to frontal and temporal lobe damage. Magnetic resonance imaging (MRI) of the head and an EEG were normal.

At the time of the patient's arrest in the late 1990s he described an elaborate system of delusions and received a hospital order disposal. Before any treatment was begun he was noted to make various clicking noises and blowing sounds. Treatments attempted for his psychosis included flupenthixol decanoate, haloperidol decanoate, olanzapine and risperidone, but with little effect; the patient reported that he developed a stammer on risperidone, with associated unusual limb and trunk movements.

Clozapine was started and prescribed up to a dose of 450 mg; however, the patient was noted to stammer and belch. He developed persistent hiccups and his facial tic worsened. A repeat MRI scan was normal and these symptoms improved as the dose of clozapine was reduced to 125 mg daily. When zuclopenthixol decanoate was prescribed instead of clozapine, because of uncertain adherence, the patient's speech improved significantly to the extent that he demonstrated no dysfluency although his dyskinetic movements remained. Unfortunately the patient's mental state deteriorated and clozapine was restarted.

At a dose of 75 mg daily (serum level 0.07 mg/l) the speech problems re-emerged. A speech and language therapy assessment revealed orofacial dyskinesia involving the lips and tongue. A 'tic-like' movement of the upper lip was observed, and sudden, involuntary contractions of the jaw resulted in the patient's teeth clicking together, characteristics associated with quick hyperkinetic dysarthria (Murdoch, 1990). The patient's speech output was characterised by occasional blocking, prolongation on word-initial sounds and repetitions of speech elements, including one-syllable words at the beginning of his speech utterances. A diagnosis of a clozapine-induced stutter was made. His family's history of speech problems may have increased his vulnerability. Despite a normal EEG, 600 mg sodium valproate daily was prescribed as an adjunct to clozapine and the patient's speech difficulties improved considerably.

Discussion

Who is at risk?

Given the widespread prescription of clozapine and the small number of case reports linking its use to stuttering, the problem seems small. However, there appear to be two groups of patients at particular risk: those who develop abnormal EEG activity on clozapine and those who have either a family history of stuttering or have themselves stuttered as a child.

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Clozapine is associated with more frequent paroxysmal EEG patterns than other antipsychotics (Koukkou *et al*, 1979). Three of the four cases in the American literature showed EEG abnormalities, including diffuse slowing and increased paroxysmal activity. Two patients suffered tonic–clonic seizures while on clozapine and in these patients co-prescription of an anticonvulsant, sodium valproate, abolished the stuttering. Sodium valproate was also effective in one of the patients we present.

Some have ascribed stuttering to abnormal micro-electrical activity, which often affects the left side of the brain, and as such treatment with anticonvulsants would make theoretical sense (Weiss *et al*, 1989).

Patients with either a family or personal history of stuttering might have a lower threshold for developing stuttering in the future and hence might be vulnerable to the effects of medication such as clozapine.

Management

An accurate diagnosis is an essential first step and this is likely to require specialist assessment by a speech and language therapist. Speech and language therapists are likely to have a key role in educating the patient, in particular in increasing their self-awareness of their speech output. Techniques such as encouraging the patient to pause before speaking and to regulate their breathing so as to speak on an egressive airstream, and working with the patient to slow down their rate of speech, may also be helpful.

The association between clozapine and stuttering appears, at least partly, to be dose related. A reduction in the dose of clozapine was enough in some patients for the stuttering to stop. This clearly needs to be balanced against the requirement to treat a patient's psychotic illness effectively. A change in medication, perhaps to another neuroleptic with fewer side-effects such as quetiapine, may be needed. An EEG examination may be helpful. If this reveals abnormalities, consideration should be given to treatment with an anticonvulsant, for example, sodium valproate.

Although clozapine is not typically associated with dystonia or extrapyramidal symptoms, in some cases stuttering appears to have presented as part of general movement side-effects (Collaborative Working Group on Clinical Trial Evaluations, 1998). In such cases tetrabenazine may be useful.

Patients typically experience more symptoms of speech dysfluency in situations where they feel anxious. Used with caution, benzodiazepines may be useful, both for their anxiolytic properties and also because of their anticonvulsant action.

Stuttering can affect a patient's self-image and inhibit their willingness to engage with others. Hence the secondary effects of stuttering should be addressed appropriately through support, reassurance and appropriate speech and language therapy.

Declaration of interest

None.

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References

ADLER, L., LEONG, S. & DELGATO, R. (1987) Drug-induced stuttering treated with propanolol. *Journal of Clinical Psychopharmacology*, **7**, 115–116.

AMERICAN PSYCHIATRIC ASSOCIATION (1994) *Diagnostic and Statistical Manual of Mental Disorders* (4th edn) (DSM–IV). APA.

ANDREWS, G., NEILSON, M. & CURLEE, R. (1988) Stuttering. *JAMA*, **260**, 1445.

COLLABORATIVE WORKING GROUP ON CLINICAL TRIAL EVALUATIONS (1998) Adverse effects of the atypical antipsychotics. *Journal of Clinical Psychiatry*, **59** (suppl. 12), 17–22.

CRAIG, A., HANCOCK, K., TRAN, Y., *et al* (2002) Epidemiology of stuttering in the communication across the entire life span. *Journal of Speech Language and Hearing Research*, **45**, 1097–1105.

DUGGAL, H. S., JAGADHEESAN, K. & NIZAMIE, S. H. (2002) Clozapine-induced stuttering and seizures. *American Journal of Psychiatry*, **159**, 315.

EBELING, T. A., COMPTON, A. D. & ALBRIGHT, D. W. (1997) Clozapine-induced stuttering. *American Journal of Psychiatry*, **154**, 1473.

GUITAR, B. E. (1985) Stuttering and stammering. *Pediatric Reviews*, **7**, 163–168.

KOUKKOU, M., ANGST, J. & ZIMMER, D. (1979) Paroxysmal EEG activity and psychopathology during the treatment with clozapine. *Psychopharmacology* **12**, 173–183.

MENKES, D. B. & UNGARVI, G. S. (1993) Adult-onset stuttering as a presenting feature of schizophrenia: restoration of fluency with trifluoperazine. *Journal of Nervous and Mental Disease*, **181**, 64–65.

MURDOCH, B. E. (1990) *Acquired Speech and Language Disorders: A Neuroanatomical and Functional Neurological Approach.* Chapman & Hall.

NURNBERG, H. G. & GREENWALD, B. (1981) Stuttering: an unusual side effect of phenothiazines. *American Journal of Psychiatry*, **138**, 386–387.

ROGERS, D. (1985) The motor disorders of severe psychiatric illness: a conflict of paradigms. *British Journal of Psychiatry*, **147**, 221–232.

SUPPRIAN, T., RETZ, W. & DECKERT, J. (1994) Clozapine-induced stuttering: epileptic brain activity. *American Journal of Psychiatry*, **156**, 1663.

TAYLOR, D., PATON, C. & KERWIN, R. (2005) *The South London and Maudsley NHS Trust Oxleas NHS Trust 2005–2006 Prescribing Guidelines*, (8th edn). Taylor & Francis.

THOMAS, P., LALAUX, N., VAIVA, G., *et al* (1994) Dose-dependent stuttering and dystonia in a patient taking clozapine. *American Journal of Psychiatry*, **151**, 1096.

WEISS, S. R. B., POST, R. M., SZELE, F., *et al* (1989) Chronic carbamazepine inhibits the development of local anaesthetic seizures kindled by cocaine and lidocaine. *Brain Research*, **497**, 72–79.

Marc Lyall Specialist Registrar in Forensic Psychiatry, **Angela Pryor** Speech and Language Therapist, ***Kevin Murray** Consultant Forensic Psychiatrist, Broadmoor Hospital, Crowthorne, Berkshire RG45 7EG, email: kevin.murray@wlmht.nhs.uk

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