BENZODIAZEPINE DEPENDENCE

Medical Research Council Headquarters File
Closed until 2014 – Opened 2005

Selected Items from File: Benzodiazepine Dependence,
File no: S1516/17 National Archives ref: FD23/4512

Submission of Additional information (CT scans)
January 1982

UNIVERSITY OF LONDON
BRITISH POSTGRADUATE MEDICAL FEDERATION

THE BETHLEM ROYAL HOSPITAL
AND
THE MAUDSLEY HOSPITAL

INSTITUTE OF PSYCHIATRY

DE CRESPIGNY PARK
DENMARK HILL
LONDON, SE5 8AF
01-703 5411

6th January 1982

Professor R. H. Cawley,
Institute of Psychiatry.

Dear Professor Cawley,

I am writing to you in your capacity as chairman of the meeting on the benzodiazepines held at the Medical Research Council on Wednesday 23rd September 1981. I am enclosing some additional information which I would have presented at that meeting if it had then been available. I understand that you are presenting the report of that meeting to the Neurosciences Board in the near future and you may consider that my supplementary information could be included.

As you will see from the table, 2 of our 14 patients have definite cortical atrophy, 5 have a borderline abnormality and the rest are normal. However, I am led to believe that the analysis of the radiologist was fairly crude and that more refined techniques might reveal further problems. Accordingly I think that the amount of abnormality is probably an underestimate.

Several of the patients are still on benzodiazepines but some have been off for quite some time.

Yours sincerely,

Malcolm Lader

M. H. Lader

cc Dr. James
Dr. Sturgess

Rec'd 18.1.82

86

ACADEMIC DEPARTMENT OF PSYCHOLOGICAL MEDICINE

(KING'S COLLEGE HOSPITAL MEDICAL SCHOOL and INSTITUTE OF PSYCHIATRY)

UNIVERSITY OF LONDON
BRITISH POSTGRADUATE MEDICAL FEDERATION

PROFESSOR ROBERT CAWLEY
DR. H. STEVEN GREER

THE BETHLEM ROYAL HOSPITAL
AND
THE MAUDSLEY HOSPITAL

INSTITUTE OF PSYCHIATRY,
DE CRESPIGNY PARK,
DENMARK HILL,
LONDON, SE5 8AF
01 - 703 5411

RHC/uml

14 January 1982

Professor Malcolm Lader
Institute of Psychiatry

Dear Malcolm

Thank you for your letter of 6 January and enclosures, in which you report information about your series of fourteen patients, previously on benzodiazapines for long periods, who had CAT scans.

I note that you have sent copies to Dr James and Dr Sturgess at the Medical Research Council. The Neurosciences Board, at its meeting on Tuesday 12 January, received the report of the ad hoc meeting we held in September 1981. I attended for that item and drew the Board's attention to the new data: so I can assure you that the Board is aware of the position.

Yours sincerely

Bob

R H Cawley

cc Dr D James
Dr E Sturgess

Do any on benzodiazepines

S.

File No.

SIS 16/17

File Note

24/2/82 87

I spoke to Prof Nader concerning the para. relating to his CAT scan studies in the minutes. I read the sentences to him & asked if he objected to the minutes being circulated to all participants at the meeting. He said that the para. was quite innocuous & could do no harm go ahead & circulate.

Julie Alston.

PATIENT	SEX	AGE	BZ. YEARS	ON/OFF BZs. AT TIME OF SCAN	RADIOLOGIST'S REPORT
G.Q.	M	37	16	OFF 2/12	Normal appearances
D.W.	M	23	3½	OFF 2/12	Normal scan
G.H.	F	40	2½	ON	Normal scan
L.M.	F	35	6	(ON)	Normal scan
M.L.	M	27	7	OFF 12/12	Normal scan
A.G.	M	76	20	ON	The sulci are marginally prominent but within normal limits considering the patient's age. The lateral ventricles are normal.
S.E.	M	58	30	ON	Scan appearances are normal for the age of the patient.
A.T.	M	50	8	ON	There is some widening of the interhemispheric fissure but no other evidence of cerebral atrophy. No focal lesion seen.
W.H.	M	43	11	OFF 10/12	There is minor prominence of the anterior inter-hemispheric fissure. There is no evidence of gross atrophy.
R.C.	M	59	16	OFF 10/12	The anterior interhemispheric fissure is widened as are occasional sulci over the frontal lobe only. The lateral ventricles are normal and the posterior aspects of the hemispheres are also normal.

PATIENT	SEX	AGE	BZ. YEARS	ON/OFF BZs. AT TIME OF SCAN	RADIOLOGIST'S REPORT
J.H.	M	34	12-15	ON	Superficially sulci are very minimally prominent considering the patient's young age. No focal abnormality is shown.
M.M.	M	40	11	ON	There is no definite cerebral atrophy present. The suloi are visible but probably just within normal limits for the patient's age.
J.M.	M	32	10	OFF 2/12	Superficial sulci in the highest most 5B cut are relatively prominent considering the patient's young age, do imply some early atrophy. The anterior interhemispheric fissure is also slightly wider than usual. Summary: There is evidence of mild cortical atrophy affecting both hemispheres superficially.
M.F.	F	39	14	ON	There is no displacement of any part of the ventricular system. The left lateral ventricle is dilated and there is widening of the left sylvian fissure. The sulci of both hemispheres are wide. There is enlargement of the superior cerebellar cistern. Conclusions: Cerebral atrophy, the left hemisphere being more affected than the right.

MEDICAL RESEARCH COUNCIL

MRC: IN CONFIDENCE

MRC 81/818
Neurosciences: January 1982

THE BENZODIAZEPINES

Report of an ad hoc meeting held on 23 September 1981

---

1. Papers

Annex 1 - minutes of the ad hoc meeting

Annex 2 - details of relevant MRC supported research

2. Background

The potential problems of overprescribing and possible dependence on benzodiazepines had been brought to the attention of the office by Professor M H Lader. After discussion with the then Board Chairman, Professor R H Cawley, it was agreed to hold an ad hoc meeting of experts in the field to review existing knowledge of the properties and usage of the drugs with special reference to the question of dependence; and in the light of research already in progress, to consider whether further studies were desirable and feasible.

The meeting took place on 23 September 1981, under the Chairmanship of Professor Cawley, and the minutes are at annex 1.

---

3. Action required

(i) Consideration of the report of the ad hoc meeting.

(ii) Decision whether to endorse the conclusions and recommendations from the meeting (annex 1 paragraphs 7.1 - 7.5).

DBM: Professor E S Paykel
S1516/17

EXTRACT FROM THE MINUTES OF THE NEUROSCIENCES BOARD MEETING OF JANUARY 1982

25. The benzodiazepines - report of an ad hoc meeting held on 23 September 1981 (MRC 81/818)

The Board received the minutes of the meeting on the benzodiazepines, which had been convened to discuss the problems of possible overprescribing and dependence on these drugs.

In introducing the paper, Professor Paykel drew attention to the studies of psychotropic drugs conducted by the General Practice Research Unit at the Institute of Psychiatry as being of particular interest. He also mentioned that extensive investigations of the neuropharmacological basis of benzodiazepines were already in progress. He then identified the two most important recommendations contained in the report. Firstly, the need for studies directed towards characterising the complex reasons for prescribing these drugs, and for producing guidelines for formulating prescribing policies. Secondly, since any prescribing of benzodiazepines carried risks as well as benefits, research should be continued into the factors which determine long-term usage and dependence, and into methods of withdrawing benzodiazepines from dependent patients.

Professor Cawley, who had been invited to attend the Board for this item as Chairman of the benzodiazepine meeting, answered questions raised by Board members. He expanded on the question of the type of research which needed to be done, laying emphasis on the related problems of tolerance and dependence and the medico-sociological factors. He suggested that research into methods of withdrawing the drugs and into non-pharmacological methods of treatment of some of the problems might be of value and agreed that research should be done to determine the actual efficacy of benzodiazepines. He emphasised the difficulty of conducting good research in this important field.

Professor Cawley presented some additional information to the Board which he had received from Professor Lader who had conducted CAT scans on some patients treated with benzodiazepines. The preliminary results suggested the need for further and more extensive studies.

The Chairman thanked Professor Cawley for attending the meeting.

Decision

The Board noted the report of an ad hoc meeting on the benzodiazepines and accepted its conclusions.

MRC Supported Research related to Benzodiazepines

MRC Establishments

1. MRC Clinical Pharmacology Unit, Oxford (Director: Professor D Grahame-Smith) - Neuropharmacology: Biochemical pharmacology of brain monoamines and effect of therapeutic agents

2. MRC Neurochemical Pharmacology Unit, Cambridge (Director: Dr L L Iversen) Neurophysiological studies of transmitter receptors in mammalian (NS) actions of psychoactive drugs

3. Professor M H Lader (ESS) London, - Psychophysiological and biochemical measures in the assessment of psychotropic drug effects.

Programme Grants

1. Professor Sir William Paton (Pharmacology, Oxford)
Chronic Effects of Centrally active Drugs and their Metabolites on Brain Chemistry and Structure.