NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Transcranial direct current stimulation (TDCS) for depression (809/1)**
Name of Specialist Advisor:	**Dr Hamish McAllister-Williams**
Specialist Society:	**Royal College of Psychiatrists**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

☒ I have never performed this procedure.

☐ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

I am not aware of any **clinical service** offering tDCS in the UK, though there is some research ongoing.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☒ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐ I have undertaken bibliographic research on this procedure.

☐ I have undertaken research on this procedure in laboratory settings (e.g. device-related research).

☐ I have undertaken clinical research on this procedure involving patients or healthy volunteers.

☒ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

I am aware of the literature on the intervention though.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☒ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

There are many different tDCS devises that have been produced and marketed. They can be bought over the internet easily. The difference in the devices makes comparison of the data in the literature extremely hard. There is uncertainty regarding optimal current to be used, placement of electrodes on the scalp and the duration and frequency of treatment. To date essentially all of the RCTs that have been conducted are small.

3.2 What would be the comparator (standard practice) to this procedure?

Antidepressants or ECT

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

As stated above, I am not aware of any clinical service using tDCS for depression in the UK

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events

Skin irritation, skin itch, hypomanic switch, exacerbation of depression

2. Anecdotal adverse events (known from experience)

Few adverse effects have been reported in clinical studies.

3. Adverse events reported in the literature (if possible please cite literature)

See above.

Reference: Brunoni AR, Ferrucci R, Fregni F, Boggio PS, Priori A. Transcranial direct current stimulation for the treatment of major depressive disorder: a summary of preclinical, clinical and translational findings. Prog Neuropsychopharmacol Biol Psychiatry. 2012 Oct 1;39(1):9-16

4.2 What are the key efficacy outcomes for this procedure?

Improvement in depressive symptoms. There have also been reports of reduction in anxiety and improvement in cognition.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

YES. To date only small RCTs conducted with inconsistent results (see review cited above). Large variation in the parameters used for the treatment

4.4 What training and facilities are required to undertake this procedure safely?

Very little training. tDCS devices are very cheap (compared to the cost of ECT or even many medication). This is a definite pro for the treatment if it can be established that it works.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

I am not aware of any large trials.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.

No

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Most definitely. Which device, magnitude of the current, placement of the electrodes, duration of treatment, frequency of treatment

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):

Montgomery Asberg Depression Rating Scale.
EQ-5D

5.2 Adverse outcomes (including potential early and late complications):

Subjective report

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

It's not ready to be "diffused"

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☒ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☒ Major.

☐ Moderate.

☐ Minor.

Comments:

It is a cheap intervention, depression is very common and a substantial proportion (30% or more) have sub-optimal outcomes with currently available treatments.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Consultancies or directorships attracting regular or occasional payments in cash or kind	☒	**YES**
	☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☒	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☒	**YES**
	☐	**NO**
Investments – any funds which include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – eg have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:

Within the last 12 months, I have undertaken consultancy work and/or received hospitality and support to attend conferences from Sunovian, Pfizer, Eli Lilly, Lundbeck and Otsaka. These companies manufacture psychotropic medication. I have not involvement with any company that manufactures tDCS

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where

the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Transcranial direct current stimulation (TDCS) for depression (809/1)**
Name of Specialist Advisor:	**Dr Mayur Bodani**
Specialist Society:	**Royal College of Psychiatrists**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

CONFIDENTIAL

1 Do you have adequate knowledge of this procedure to provide advice?

☑ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☐ Yes.

☑ No. If no, please enter any other titles below.

Comments: TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) FOR MILD, MODERATE OR SWERE DEPRESSION

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☑ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

RESEARCH EVIDENCE FOR EFFICACY IS LIMITED

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

- [x] I have never performed this procedure.
- [ ] I have performed this procedure at least once.
- [ ] I perform this procedure regularly.

Comments:

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

- [x] I have never taken part in the selection or referral of a patient for this procedure.
- [ ] I have taken part in patient selection or referred a patient for this procedure at least once.
- [ ] I take part in patient selection or refer patients for this procedure regularly.

Comments:

CLINICAL CARE PATHWAYS FOR REFERRAL FOR TREATMENT ARE LIMITED TO CENTRES WITH RESEARCH INTERESTS IN TDCS

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

- [x] I have undertaken bibliographic research on this procedure.
- [ ] I have undertaken research on this procedure in laboratory settings (e.g. device-related research).
- [ ] I have undertaken clinical research on this procedure involving patients or healthy volunteers.
- [ ] I have had no involvement in research on this procedure.
- [ ] Other (please comment)

Comments:

CONFIDENTIAL

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☑ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

REMAINS NOVEL, WITH VARIATIONS eg rTMS. MANY UNANSWERED QUESTIONS eg. TARGET, POSITIONING, OPTIMAL DOSE, OPTIMAL TIME PERIOD, CASE SELECTION.

3.2 What would be the comparator (standard practice) to this procedure?

ECT (if Neurostimulation being considered as a comparator)

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☑ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events

Headache
Tingling or twitching of facial muscles
Scalp irritation
Light headedness

} unable to cite evidence of incidence.

CONFIDENTIAL

2. Anecdotal adverse events (known from experience)

None from experience

3. Adverse events reported in the literature (if possible please cite literature)

Known risk of seizure especially re: rTMS of the order of 20 seizures in approximately 300,000 or more treatment and research sessions (Mark George et al, Curr. Opin. Psychiatry, 2013; 26(1): 13-18).

4.2 What are the key efficacy outcomes for this procedure?

- IMPROVEMENT IN DEPRESSION OUTCOME SCALES.
- EFFECTIVENESS IN TREATMENT RESISTANCE.
- ? IMPROVEMENT IN OTHER PARAMETERS eg. COGNITIVE FUNCTION, PAIN, NEUROLOGICAL SYMPTOMS

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

? LONG TERM USE SIDE-EFFECTS

? LONG TERM SUSTAINED BENEFITS.

? POSITION AS A TREATMENT ALONGSIDE OTHER ORTHODOX TREATMENTS eg. ANTIDEPRESSANT, ECT, CBT

4.4 What training and facilities are required to undertake this procedure safely?

- TRAINING IN USE OF EQUIPMENT.
- MANAGEMENT OF POSSIBLE SIDE-EFFECTS
- IDEALLY HOSPITAL-BASED AT INITIATION IN SETTING WITH SPECIALIST EXPERTISE & EXPERIENCE.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

MULTIPLE CENTRES ARE INTERESTED IN THIS MODE OF TREATMENT AND APPLICABILITY TO A RANGE OF CONDITIONS (BOTH CLINICAL eg. MAUDSLEY / IOP; AND RESEARCH eg. IN THE UK, UNIVERSITY OF KENT).
NOT AWARE OF SPECIFIC TRIALS.

CONFIDENTIAL

4.6 **Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.**

NO.

4.7 **Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?**

INDIVIDUAL STUDIES HAVE GENERALLY BEEN UNDERPOWERED.
META-ANALYSIS DATA IS LIMITED.
LARGER RCD TRIALS NEEDED.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 **Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):**

BDI / MADRS (depression)
HADS / BAI (Anxiety & depression)
CORE/GCI / EQ5D (global impression / quality)
ACE-III (brief cognitive screening)

5.2 **Adverse outcomes (including potential early and late complications):**

early : side-effects
eg. headaches
skin irritation
Cognitive change

late : Seizure.
failure to maintain benefit.
? need for help-loss ?

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

WITHIN NEXT 5 YEARS TDCS LIKELY TO BECOME INCREASINGLY AVAILABLE AND USED AS AN ADJUNCTIVE TREATMENT IN MDD AND MILDER FORMS OF DEPRESSION.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

- [x] Most or all district general hospitals.
- [ ] A minority of hospitals, but at least 10 in the UK.
- [ ] Fewer than 10 specialist centres in the UK.
- [ ] Cannot predict at present.

Comments:

WITH INCREASING AWARENESS, LOW COST, LOW SIDE-EFFECT PROFILE, AND INCREASING RANGE OF APPLICABLE CONDITIONS.

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

- [ ] Major.
- [x] Moderate.
- [ ] Minor.

Comments:

. LOW COST RESOURCES
. FAIRLY SHORT TRAINING
. POSSIBLE TO DISSEMINATE TRAINING AND USE TO NON-MEDICAL STAFF eg. specialist nurses.

CONFIDENTIAL

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

Publications in this area are rapidly increasing but trial data is limited.

A Cochrane review could be initiated at an early stage.

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

CONFIDENTIAL

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐ YES ☑ NO
Fee-paid work – any work commissioned by the healthcare industry – **this includes income earned in the course of private practice**	☐ YES ☑ NO
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐ YES ☑ NO
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐ YES ☑ NO
Investments – any funds which include investments in the healthcare industry	☐ YES ☑ NO
Do you have a **personal non-pecuniary** interest – eg have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐ YES ☑ NO

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐ YES ☑ NO
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐ YES ☑ NO

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:

CONFIDENTIAL

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Transcranial direct current stimulation (TDCS) for depression (809/1)**
Name of Specialist Advisor:	**Dr Philip Wilkinson**
Specialist Society:	**Royal College of Psychiatrists**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

☐ I have never performed this procedure.

☒ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

I have recently introduced the procedure within out Trust.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☒ I have undertaken bibliographic research on this procedure.

☐ I have undertaken research on this procedure in laboratory settings (e.g. device-related research).

☐ I have undertaken clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☒ Other (please comment)

Comments:

I have observed the procedure in use by academic colleagues conducting studies with healthy volunteers. I have collaborated with local colleagues and overseas experts in grant applications for trials of tDCS in depression.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☒ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

There are good safety data as the procedure has been in use in non-clinical applications for some time. The therapeutic use in depression is relatively new.

3.2 What would be the comparator (standard practice) to this procedure?

Pharmacotherapy (antidepressant medication); psychological treatment; electroconvulsive therapy.

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

I believe there to be only 2 or 3 in the country.

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events

Precipitation of seizures; interference with implanted electrical devices (brain sitmulators, cardiac pacemakers).

2. Anecdotal adverse events (known from experience)

Skin tingling and burning sensation (common).

Induction of phosphenes ('flashing lights') with anterior stimulation positions.

3. Adverse events reported in the literature (if possible please cite literature)

Skin tingling (71%), itching (30%), headache (12%), burning under the electrodes, difficulties in concentrating, acute mood changes (including mania).

Brunoni AR, Amadera J, Berbel B, Volz MS, Rizzerio BG, Fregni F. A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. The International Journal of Neuropsychopharmacology. 2011;14(08):1133-45.

4.2 What are the key efficacy outcomes for this procedure?

Change in depression severity/remission of depression

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Small number of RCTs to date so efficacy and effect size relative to other treatments uncertain.

Shiozawa P, Fregni F, Benseñor IM, Lotufo PA, Berlim MT, Daskalakis JZ, et al. Transcranial direct current stimulation for major depression: an updated systematic review and meta-analysis. International Journal of Neuropsychopharmacology. 2014;19(9):1443-52.

4.4 What training and facilities are required to undertake this procedure safely?

This is relatively straightforward. The equipment is quite cheap (c £6k per stimulator) and easily portable so can be used anywhere, including (potentially) in care homes and patients' homes. Consumables costs are very low. There are even devices that patients can apply themselves.

Training requires observation of a small number of sessions, and some initial supervision, but this is straightforward. In our Trust, I am delivering treatment in the

inpatient unit and outpatient clinic, and am teaching other medical staff and nursing staff how to perform the procedure.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

There are numerous ongoing trials (as listed in ClinicalTrials.gov). Major centres are in USA, Brazil, Australia, and Germany.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.

No.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

There is uncertainty about the optimal treatment parameters, i.e. electrode size and positioning; current strength; duration of stimulation; number of sessions, including taper sessions. This is the focus of some of the trials.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):

Depression measures (e.g. MADRS, HDRS)

Cognitive measures (e.g. MOCA, n-back)

5.2 Adverse outcomes (including potential early and late complications):

Manic switch (eg YMRS)

Adverse events questionnaire (AEQ)

Brunoni AR, Amadera J, Berbel B, Volz MS, Rizzerio BG, Fregni F. A systematic review on reporting and assessment of adverse effects associated with transcranial

direct current stimulation. The International Journal of Neuropsychopharmacology. 2011;14(08):1133-45.

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

I would expect a gradual diffusion of the procedure over the next 5 to 10 years if future trials support its efficacy in depression

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☒ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

As a non-invasive, safe, cheap, and portable treatment, it should suitable for widespread dissemination not just in hospital services but in community settings too.

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☒ Moderate.

☐ Minor.

Comments:

It is unlikely ever to be a first-line treatment for depression, replacing pharmacotherapy and psychotherapy. However, as it acts by a different mechanism to these modalities (i.e. neuromodulation) it could extend the armoury of interventions available to patients. It may also prove beneficial for patients who do not respond to current interventions, but this has not yet been convincingly demonstrated.

It would be a safe treatment option for patients who need to avoid pharmacotheraBrunoni AR, Amadera J, Berbel B, Volz MS, Rizzerio BG, Fregni F. A systematic review on reporting and assessment of adverse effects associated with

transcranial direct current stimulation. The International Journal of Neuropsychopharmacology. 2011;14(08):1133-45.
epy e.g. older patients unable to tolerate medication; pregnant patients.

It is unlikely to be as efficacious as ECT so seems unlikely to replace ECT in the treatment of severe, life-threatening depression. However, it may be a more acceptable treatment to those patients with drug-refractory depression who currently are treated with ECT.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

In our Neurobiology of Ageing Group in Oxford (led by Professor Klaus Ebmeier), we are particularly interested in the potential benefits of tDCS for older depressed patients. Late life depression can be associated with disruption of brain white matter tracts, and tDCS may have the potential to help restore connectivity in these structures. However, this requires evaluation. There are important potential benefits for older people if the procedure is shown to improve enhance mood as well as improve the cognitive deficits associated with late life depression.

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	☒	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☒	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**
Investments – any funds which include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – eg have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where

the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.