though successful in other disciplines (e.g. obstetrics)[39]. This is despite the negative long-term effects of OT treatment observed in non-human adolescent mammals[40], and the presence of OT and cross-reactive vasopressin (AVP) receptors throughout the body[41] that are involved in a variety of homeostatic functions related to observed side effects[42].

It is an aim of the present invention to provide for improved efficacy in the intranasal administration of oxytocin (OT), especially for the modulation of social cognition and/or behavior, and other peptides, including Orexin-A, especially for the treatment of narcolepsy, and insulin, especially for the treatment of diabetes.

Summary of the Invention

According to a first aspect of the present invention, there is provided a delivery device for and method of modulating a condition relating to social cognition and/or behaviour in a human subject using oxytocin, non-peptide agonists thereof and/or antagonists thereof, comprising: providing a nosepiece to a first nasal cavity of the subject; and providing a supply unit for administering less than 24IU of oxytocin, non-peptide agonists thereof and/or antagonists thereof through the nosepiece to an upper region posterior of the nasal valve which is innervated by the trigeminal nerve.

According to a second aspect of the present invention, there is provided delivery device or method of modulating a condition in a human subject using a peptide, non-peptide agonists thereof and/or antagonists thereof, comprising: providing a nosepiece to a first nasal cavity of the subject; and providing a supply unit for administering less than 24IU of a peptide, non-peptide agonists thereof and/or antagonists thereof through the nosepiece to an upper region posterior of the nasal valve which is innervated by the trigeminal nerve.

There is provided a method of modulating conditions relating to social cognition and/or behaviour in a human subject using oxytocin, non-peptide agonists thereof and/or antagonists thereof, comprising: providing a nosepiece to a first nasal cavity of the subject; and administering less than 24IU of oxytocin, non-peptide agonists thereof and/or antagonists thereof to an upper region posterior of the nasal valve which is innervated by the trigeminal nerve.

There is provided a method of modulating a condition in a human subject using a peptide, non-peptide agonists thereof and/or antagonists thereof, comprising: providing a nosepiece to a first nasal cavity of the subject; and administering less than 24IU of a peptide, non-peptide agonists thereof and/or antagonists thereof through the nosepiece to an upper region posterior of the nasal valve which is innervated by the trigeminal nerve.

There is provided a nosepiece for delivering substance to a nasal cavity of a subject, the nosepiece comprising: a first, inner body part; and a second, outer body part which is disposed about at

least a distal portion of the inner body part and defines a tip; wherein the inner body part comprises a base portion which defines a flow passage therethrough, and a projection at the distal end thereof which supports the tip and confers a rigidity in the sagittal direction, which enables the tip to open fleshy tissue at an upper region of the nasal valve and thereby expand an open area of the nasal valve, and a flexibility in a lateral direction, orthogonal to the sagittal plane, which facilitates insertion of the tip into the nasal valve.

There is provided a nosepiece for delivering substance to a nasal cavity of a subject, the nosepiece comprising a body part which comprises a base portion which defines a flow passage therethrough, and a projection at a distal end of the base portion which at least in part provides a tip of the nosepiece and confers a rigidity in the sagittal direction, which enables the tip to open fleshy tissue at an upper region of the nasal valve and thereby expand an open area of the nasal valve, and a flexibility in a lateral direction, orthogonal to the sagittal plane, which facilitates insertion of the tip into the nasal valve.

Description of the Figures

Preferred embodiments of the present invention will now be described hereinbelow by way of example only with reference to the accompanying drawings, in which:

Figures 1(a) to (c) illustrate a delivery device in accordance with one embodiment of the present invention;

Figures 2(a) to (e) illustrate perspective, lateral, front, underneath and longitudinal sectional views (along section A-A) of the nosepiece of the device of Figures 1(a) to (c);

CLAIMS

1. A delivery device for and method of modulating a condition relating to social cognition and/or behaviour in a human subject using oxytocin, non-peptide agonists thereof and/or antagonists thereof, comprising:
providing a nosepiece to a first nasal cavity of the subject; and
providing a supply unit for administering less than 24IU of oxytocin, non-peptide agonists thereof and/or antagonists thereof through the nosepiece to an upper region posterior of the nasal valve which is innervated by the trigeminal nerve.

2. The delivery device or method of claim 1, further comprising:
providing a mouthpiece through which the subject exhales to cause closure of the oropharyngeal velum of the subject, optionally the mouthpiece is fluidly connected to the nosepiece, whereby an exhalation breath is delivered from the mouthpiece and through the nosepiece into the first nasal cavity, optionally an air flow created by the exhalation breath is delivered around a posterior margin of the nasal of the subject and out of a second nasal cavity of the subject.

3. The delivery device or method of claim 1, further comprising:
providing a gas flow through the nosepiece into the first nasal cavity during administration of the oxytocin, non-peptide agonists thereof and antagonists thereof, optionally (i) the gas flow is separate to an air flow created by an exhalation breath, or (ii) the gas flow created by the exhalation breath is delivered around a posterior margin of the nasal of the subject and out of a second nasal cavity of the subject.

4. The delivery device or method of claim 1, wherein:
   (i) the oxytocin, non-peptide agonists thereof and/or antagonists thereof is delivered as a liquid;

(ii) the oxytocin, non-peptide agonists thereof and/or antagonists thereof is delivered as a liquid spray;

(iii) the oxytocin, non-peptide agonists thereof and/or antagonists thereof is delivered as a powder;

(iv) the oxytocin, non-peptide agonists thereof and/or antagonists thereof is delivered as a powder spray;

(v) less than 15 IU of oxytocin, non-peptide agonists thereof and/or antagonists thereof is administered;

(vi) less than 12 IU of oxytocin, non-peptide agonists thereof and/or antagonists thereof is administered;

(vii) less than 10 IU of oxytocin, non-peptide agonists thereof and/or antagonists thereof is administered;

(viii) greater than 1 IU of oxytocin, non-peptide agonists thereof and/or antagonists thereof is administered;

(ix) greater than 2 IU of oxytocin, non-peptide agonists thereof and/or antagonists thereof is administered; or

(x) greater than 4 IU of oxytocin, non-peptide agonists thereof and/or antagonists thereof is administered.

5. The delivery device or method of claim 1, further comprising:

expanding the nasal valve within the first nasal cavity, optionally:

(i) the nasal valve is expanded by insertion of the nosepiece from an unexpanded cross-sectional area of at least 20 mm^2;

(ii) the nasal valve is expanded by insertion of the nosepiece from an unexpanded cross-sectional area of at least 40 mm^2;

(iii) the nasal valve is expanded by insertion of the nosepiece from an unexpanded cross-sectional area of at least 60 mm^2;

(iv) the nasal valve is expanded by insertion of the nosepiece from an unexpanded cross-sectional area of at least 70 mm^2;

(v) the nasal valve is expanded by insertion of the nosepiece from an unexpanded cross-sectional area of at least 80 mm^2;

(vi) the nasal valve is expanded by insertion of the nosepiece from an unexpanded cross-sectional area of at least 90 mm^2;

(vii) the nasal valve is expanded by insertion of the nosepiece from an unexpanded cross-sectional area of at least 100 mm^2;

(viii) the nasal valve is expanded by insertion of the nosepiece to have a cross-sectional area which is 1.5 times an unexpanded cross-sectional area of the nasal valve;

(ix) the nasal valve is expanded by insertion of the nosepiece to have a cross-sectional area which is 1.75 times an unexpanded cross-sectional area of the nasal valve;

(x) the nasal valve is expanded by insertion of the nosepiece to have a cross-sectional area which is 2 times an unexpanded cross-sectional area of the nasal valve;

(xi) the nasal valve is expanded by insertion of the nosepiece to have a cross-sectional area of at least 100 mm^2;

(xii) the nasal valve is expanded by insertion of the nosepiece to have a cross-sectional area of at least 120 mm^2;

(xiii) the nasal valve is expanded by insertion of the nosepiece to have a cross-sectional area of at least 150 mm^2;

(xiv) the nasal valve is expanded by insertion of the nosepiece to have a cross-sectional area of at least 180 mm^2;

(xv) the nasal valve is expanded by insertion of the nosepiece to have a cross-sectional area of at least 200 mm^2; or

(xvi) the nosepiece includes a tip which extends into the nasal valve and acts to expand the nasal valve.

6. The delivery device or method of claim 5, wherein the nosepiece comprises a body part which comprises a base portion which defines a flow passage therethrough, and a projection at a distal end of the base portion which at least in part provides the tip of the nosepiece and confers a rigidity in the sagittal direction, which enables the tip to open fleshy tissue at an upper region of the nasal valve and thereby expand an open area of the nasal valve, and a flexibility in a lateral direction, orthogonal to the sagittal plane, which facilitates insertion of the tip into the nasal valve, optionally (i) the body part is

formed of a plastics material, optionally an acrylonitrile butadiene styrene (ABS) plastic, or (ii) the nosepiece further comprises an outer body part which is disposed about at least the projection, optionally the outer body part is formed of a resilient material, optionally a rubber or elastomeric material, optionally the outer body part is formed of a thermoplastic elastomer (TPE).

7. The delivery device or method of claim 6, wherein:
   (i) the base portion defines a substantially annular surface at a distal end thereof which tapers or is inclined in relation to the longitudinal axis of the nosepiece, such that the surface of the base portion is inclined from the projection in a proximal direction, whereby the base portion is shorter at that side which is opposite to the projection; or
   (ii) the projection extends axially in substantially parallel and offset relation to the longitudinal axis of the nosepiece.

8. The delivery device or method of claim 6, wherein the projection comprises a flat element, optionally in the form of a blade, with a length (d1) in the sagittal direction being greater than a length (d2) in the lateral direction, optionally:
   (i) the length (d1) in the sagittal direction is 1.5 times greater than the mean length (d2) in the lateral direction;
   (ii) the length (d1) in the sagittal direction is 1.7 times greater than the mean length (d2) in the lateral direction;
   (iii) the length (d1) in the sagittal direction is 1.9 times greater than the mean length (d2) in the lateral direction;
   (iv) the length (d1) in the sagittal direction is 2 times greater than the mean length (d2) in the lateral direction;
   (v) the projection has a length (d1) in the sagittal direction of less than 3 mm, optionally less than 2.5 mm;
   (vi) the projection has a length (d1) in the sagittal direction of greater than 1.5 mm;

(vii) the projection has a length (d2) in the lateral direction of less than 1.5 mm, optionally less than 1.25 mm;

(viii) the projection has a length (d2) in the lateral direction of greater than 0.5 mm, optionally greater than 0.75 mm;

(ix) the projection has a main body section and a tip section which has a shorter length (d3) in the sagittal direction than the length (d1) of the main body section, optionally defining a step at an inner edge thereof; or

(x) the projection has a tapering lateral cross-section along a longitudinal extent thereof, with the length (d2) in the lateral direction reducing in cross-section along the longitudinal extent in a direction towards the distal end thereof.

9. The delivery device or method of claim 1, wherein the administration is performed in a single delivery or a plurality of deliveries, optionally the administration is done as (i) a once-daily administration or (ii) a twice-daily administration.

10. The delivery device or method of claim 1, wherein the administration is of (i) oxytocin, (ii) a non-peptide oxytocin agonist or WAY-267,464, (iii) an oxytocin antagonist, (iv) desglycinamide oxytocin, or (v) an analogue or derivative of oxytocin, optionally carbetocin or demoxytocin.

11. The delivery device or method of claim 1, wherein the administration is of both peptide and non-peptide oxytocin.

12. The delivery device or method of claim 1, wherein the administration is targeted to provide for nose-to-brain (N2B) transport, optionally the substance is targeted to provide for reduced systemic delivery.

13. The delivery device or method of claim 1, wherein the administration provides for (i) less than a 20% change in the plasma concentration

of vasopressin, (ii) less than a 10% change in the plasma concentration of vasopressin, (iii) less than a 5% change in the plasma concentration of vasopressin, or (iv) substantially no change in the plasma concentration of vasopressin.

14. A delivery device or method of modulating a condition in a human subject using a peptide, non-peptide agonists thereof and/or antagonists thereof, comprising:
providing a nosepiece to a first nasal cavity of the subject; and
providing a supply unit for administering less than 24IU of a peptide, non-peptide agonists thereof and/or antagonists thereof through the nosepiece to an upper region posterior of the nasal valve which is innervated by the trigeminal nerve.

15. The delivery device or method of claim 14, wherein the peptide comprises (i) oxytocin, such as for modulating a condition relating to social cognition and/or behaviour, (ii) Orexin-A, such as for the treatment of narcolepsy, or (iii) insulin, such as for the treatment of diabetes.