[0018] Concerns have been expressed over possible side effect of some of the medications used to treat anxiety disorders, particularly the benzodiazepines. Common side effects associated with these medications, which may decrease over the course of treatment, include sedation, fatigue, ataxia, slurred speech, and amnesia, the latter two effects observable if the agents are used in high doses, or are otherwise abused. Benzodiadepines have also the potential for producing drug dependence (i.e. physiological or behavioral symptoms after discontinuation of use), and in this context, suffer from the same drawbacks recited with respect to the narcotic agents discussed.

[0019] There is therefore a continuing need for new agents that are effective and safe anxiolytics. More specifically, a need exists for the development of a dosage form and composition for the administration of a medication that can function as an anxiolytic, and that leaves no anesthetic effect, and that does not induce addiction or dependence or potential for respiratory or circulatory collapse/impairment. Also, it is toward the achievement of the aforementioned objectives that the present invention is directed.

SUMMARY ~~OF INVENTION~~

[0020] In accordance with the present ~~invention~~disclosure, a method for inhibiting or treating the development of anxiety in a subject is disclosed which comprises administering to the subject an anxiolytic agent comprising an NMDA receptor antagonist, in an amount which is non-anesthetic and mildly analgesic. More particularly, the NMDA receptor antagonist may be prepared in a composition in an exemplary unit dosage amount of between about 0.05mg/kg to 0.5mg/kg, with 0.1mg/kg to about 0.3mg/kg, being exemplary.

[0021] The present method comprises the administration of the anxiolytic agent by a variety of routes, including intravenous, intranasal, transdermal, transmucosal and transbuccal administration.

[0022] The ~~invention~~ disclosure relates to the use of NMDA receptor antagonists, and preparations containing the same, and the manufacture of pharmaceutical compositions, all of which can be used to relieve natural occurrences of anxiety as well as symptoms of anxiety disorders.

[0022a] In one aspect, there is provided use of an NMDA receptor antagonist in the manufacture of a medicament for inhibiting, ameliorating or treating the development of anxiety in a subject, wherein the NMDA receptor antagonist is in an amount of from about 0.1mg/kg to 0.3mg/kg.

[022b] In one aspect, there is provided a pharmaceutical composition which comprises about 0.05 mg/kg to about 0.5 mg/kg ketamine hydrochloride, wherein the composition is sub-anesthetic and hypo-analgetic, and is administered as a premedication.

[022c] In one aspect, there is provided an anxiolytic composition for the prevention, amelioration and/or treatment of anxiety in a subject comprising a sub-anesthetic and hypo-analgetic dosage of an NMDA receptor antagonist.

[0023] More particularly, the present ~~invention~~ disclosure is concerned with anxiety that is of a less severe nature, and could be best described as the feeling of uneasiness and apprehension that is frequently experienced by normal individuals. This form of anxiety is distinguishable from the clinical or psychiatric state that has been discussed in detail above. While the disorders described here can interfere with a person's level of functioning, but can be effectively treated by use of the present ~~invention~~disclosure. The compounds of the disclosure~~invention~~ are particularly useful for treating anxiety

that is not severe. A person with occasional panic attacks, for example, may be treated with compounds of the disclosure~~invention~~ even though the person may not have panic disorder; the person need not wait to suffer from repeated panic attacks or be incapacitated by them before starting treatment with the compounds of the present disclosure~~invention~~. Similarly, a patient suffering from a mild form of acute stress disorder may be treated with compounds of the disclosure~~invention~~; one need not wait for the acute disorder to progress to posttraumatic stress disorder. What matters is only that a person seeking treatment for anxiety finds the anxiety unpleasant and wishes to alleviate it and/or prevent it from occurring.

[0024] The composition, formulation and device of the disclosure~~invention~~ is likewise embodied in a kit, where, for example, a suitable unit dosage form may be prepared in a single-use aerosol or multi dose spray device for personal storage and immediate use.

[0024a] In one aspect, there is provided a unit dose of a pharmaceutical composition which comprises an aqueous solution containing about 0.05 mg/kg to about 0.5 mg/kg ketamine hydrochloride, wherein the unit dose is sub-anesthetic and hypo-analgetic, and wherein said dose is administered as a premedication.

[0025] Accordingly, it is a principal object of the present disclosure~~invention~~ to prepare a formulation and composition for the administration of an anxiolytic that prevents, ameliorates or treats anxiety in a subject without causing cognitive impairment and little or no negative impact on patient function/performance.

[0026] It is accordingly, a further object of the present disclosure~~invention~~ to provide a formulation, composition and method of administration as aforesaid, that offers rapid onset and relief with no negative after effects.

[0027] It is a yet further object of the present disclosure~~invention~~ to provide a unit dosage form and corresponding kit including the formulation and composition of the present disclosure~~invention~~ disposed within separable containers within an administration device such as a syringe.

[0028] Other objects and advantages will become apparent to those skilled in the art from a review of the ensuing detailed description.

DETAILED DESCRIPTION OF THE INVENTION

[0029] In accordance with the present invention, the foregoing objects and advantages are readily attained.

[0030] In its broadest aspect, the present invention relates to a composition and a formulation that unexpectedly functions as a safe and effective anxiolytic. The present invention comprises the administration of an NMDA receptor antagonist, such as ketamine at a sub-anesthetic dose, for use as an anxiolytic that is particularly suited to treat the mild form of anxiety of interest herein. The method, composition and dosage form are specifically intended for use with adult subjects, from adolescent age and older.

WHAT IS CLAIMED IS:

1. ~~A method for inhibiting, ameliorating or treating the development of anxiety in a subject, comprising administering to said subject~~Use of an NMDA receptor antagonist in the manufacture of a medicament for inhibiting, ameliorating or treating the development of anxiety in a subject, wherein the NMDA receptor antagonist is in an amount of from about 0.1mg/kg to 0.3mg/kg.
2. The use~~method~~ of claim 1 wherein the NMDA receptor antagonist comprises ketamine, and pharmaceutically acceptable salts thereof.
3. The use~~method~~ of claim 2 wherein said the NMDA receptor antagonist comprises ketamine hydrochloride.
4. The use~~method~~ of claim 1 wherein the NMDA receptor antagonist is to be administered intranasally.
5. The use~~method~~ of claim 1 wherein the NMDA receptor antagonist is to be administered transbuccally.
6. The use~~method~~ of claim 1 wherein the NMDA receptor antagonist is to be administered transdermally.
7. The use~~method~~ of claim 1 wherein the NMDA receptor antagonist is to be administered intravenously.
8. The use~~method~~ of claim 1, wherein the anxiety is associated with generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, a phobic disorder, acute stress disorder, post-traumatic stress disorder, or mixed anxiety-depression.
9. The use~~method~~ of claim 1 wherein said NMDA receptor antagonist is to be administered prior to a medical or dental procedure.
10. The use~~method~~ of claim 7 wherein said NMDA receptor antagonist is to be administered from about 30 minutes to about 2 minutes prior to said medical or dental procedure.
11. The use~~method~~ of claim 1 wherein said NMDA receptor antagonist is to be administered prior to the administration of electroshock therapy.
12. A pharmaceutical composition which comprises ~~containing~~ about 0.05 mg/kg to about 0.5 mg/kg ketamine hydrochloride, wherein the composition is sub-anesthetic and hypo-analgetic, and is administered as a premedication.
13. The pharmaceutical composition of claim 11, further comprising a suitable carrier selected from the group consisting of water, saline, bicarbonate, sucrose and mixtures thereof.
14. A composition according to claim11 wherein said composition is prepared in as an aqueous solution.