to dextrorphan is dominant in the majority of the population and is the principle behind using dextromethorphan as a probe to phenotype individuals as CYP2D6 extensive and poor metabolizers (Kupfer et al., Lancet. 1984;2:517-518; Guttendorf et al., Ther. Drug Monit. 1988;10:490-498). Approximately 7% of the Caucasian population shows the poor metabolizer phenotype, while the incidence of poor metabolizer phenotype in Chinese and Black African populations is even lower (Droll et al., Pharmacogenetics. 1998;8:325-333). A study examining the ability of dextromethorphan to increase pain threshold in extensive and poor metabolizers found antinociceptive effects of dextromethorphan were significant in poor metabolizers but not in extensive metabolizers (Desmeules et al., J. Pharmacol. Exp. Ther. 1999;288:607-612). The results are consistent with direct effects of parent dextromethorphan rather than the dextrorphan metabolite on neuromodulation.

SUMMARY

[011] As described above, there remains an urgent need for additional or improved forms of treatment for agitation, aggression and/or associated symptoms in subjects with Alzheimer's disease. This disclosure describes methods of treating agitation and/or aggression and/or associated symptoms in subjects with Alzheimer's disease without an increased risk of serious adverse effects.

[012] In one aspect, the present disclosure refers to the use of a combination of d6-dextromethorphan and quinidine in the manufacture of a medicament for treating dementia-related agitation and/or aggression in a subject. In another example, there is disclosed a method for treating agitation and/or aggression and/or associated symptoms in subjects with dementia by administering a dextromethorphan compound in combination with a CYP2D6 inhibitor, such as quinidine (Q). The disclosure also encompasses the use of pharmaceutically acceptable salts of either or both the dextromethorphan compound and quinidine in the

WHAT IS CLAIMED:

1. Use of a combination of d6-dextromethorphan and quinidine in the manufacture of a medicament for treating dementia-related agitation and/or aggression in a subject.

2. The use according to claim 1, wherein the dementia is of the Alzheimer's type.

3. The use according to any preceding claim, wherein the d6-dextromethorphan is to be administered in an amount ranging from 10 mg to 200 mg per day.

4. The use according to any preceding claim, wherein the quinidine is to be administered in an amount ranging from 0.05 mg to less than 50 mg per day.

5. The use according to any preceding claim, wherein the d6-dextromethorphan is in a form of d6-dextromethorphan hydrobromide.

6. The use according to any preceding claim, wherein the quinidine is in a form of quinidine sulfate.

7. The use of according to any preceding claim, wherein the d6-dextromethorphan and the quinidine are to be administered in a unit dosage form comprising

(i) 24 mg d6-dextromethorphan hydrobromide and 4.75 mg quinidine sulfate; or

(ii) 34 mg d6-dextromethorphan hydrobromide and 4.75 mg quinidine sulfate; or

(iii) 18 mg d6-dextromethorphan hydrobromide and 4.9 mg quinidine sulfate; or

(iv) 28 mg d6-dextromethorphan hydrobromide and 4.9 mg quinidine sulfate; or

(v) 30 mg d6-dextromethorphan hydrobromide and 4.9 mg quinidine sulfate; or

(vi) 24 mg d6-dextromethorphan hydrobromide and 4.9 mg quinidine sulfate; or

(vii) 34 mg d6-dextromethorphan hydrobromide and 4.9 mg quinidine sulfate.

8. The use according to any preceding claim, wherein the d6-dextromethorphan and the quinidine are to be administered as one combined dose per day.

9. The use according to any one of claims 1-7, wherein the d6-dextromethorphan and the quinidine are to be administered as two or more combined doses per day.

10. The use according to any preceding claim, wherein the d6-dextromethorphan and the quinidine are to be administered in a tablet unit dosage form or a capsule unit dosage form.

11. The use according to any of claims 1-6 and 8-10, wherein the d6-dextromethorphan is to be administered in an amount of about 42 mg and the quinidine is to be administered in an amount of 4.9 mg.

12. The use according to any of claims 1-6 and 8-10, wherein the d6-dextromethorphan is to be administered in an amount of about 43 mg and the quinidine is to be administered in an amount of 4.9 mg.