EFFECTIVENESS OF VORTIOXETINE FOR EMOTIONAL BLUNTING IN PATIENTS WITH INADEQUATE RESPONSE TO SSRI/SNRI

PSYCHIATRY EDUCATION FORUM'S
Journal Club

DR. HARVINDER SINGH

TABLE OF CONTENTS

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Effectiveness of Vortioxetine on Emotional Blunting in Patients with Major Depressive Disorder with inadequate response to SSRI/SNRI treatment

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Affiliations – collapse

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EMOTIONAL BLUNTING WITH ANTIDEPRESSANTS

- Common with SSRIs & SNRIs: at higher doses
- Increase risk of medication discontinuation
- Affect social functioning & prevent full recovery

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ANHEDONIA VS EMOTIONAL BLUNTING

	ANHEDONIA	EMOTIONAL BLUNTING
ABILITY TO EXPERIENCE PLEASURE	DECREASED	DECREASED
EXPERIENCE NEGATIVE EMOTIONS	PERCEPTION HEIGHTENED	PERCEPTION BLUNTED
ANTIDEPRESSANTS	BENEFICIAL	CAUSE/WORSEN

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MECHANISM?

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- Serotonergic effects on frontal lobes and/or
- Serotonergic modulation of midbrain dopaminergic systems, which project to the prefrontal cortex.

VORTIOXETINE?

J PSYCHIATR PRACT. 2004 MAY; 10(3):196-9.
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WHAT DID AUTHORS DO?

INCLUSION CRITERIA:

MDD DIAGNOSIS IN 18-65 YEAR OLD:

- Current depressive episode of < 12 months

SCREENING SCALES:

- MADRS>21 and <29
- Oxford Depression Questionnaire(ODQ) ≥50

PARTIAL RESPONSE TO SSRI/SNRI:

- at least 6 weeks with inadequate response

EMOTIONAL BLUNTING QUESTION:

- "Emotional effects vary, but may include, for example, feeling emotionally 'numbed' or 'blunted' in some way; lacking positive emotions or negative emotions; feeling detached from the world around you; or 'just not caring' about things that you used to care about. Have you experienced such emotional effects during the last 6 weeks?".

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OUTCOME MEASURES

PRIMARY OUTCOME MEASURE

Oxford Depression Questionnaire (ODQ) total score

SECONDARY OUTCOME MEASURE

MADRS Total Score & 5-item MADRS Anhedonia Subscale Score

CGI-Severity of Illness (CGI-S)

Motivation and Energy Inventory (MEI)

Sheehan Disability Scale (SDS)

Digit Symbol Substitution Test (DSST)

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OXFORD DEPRESSION QUESTIONNAIRE (ODQ)

Patient-reported, 26-item rating scale

Assess five dimensions of emotional blunting:

- Not Caring (NC)
- Emotional Detachment (ED)
- Positive Reduction (PR)
- General Reduction (GR)
- Antidepressant as Cause (AC)

Total score range: 26-130

J AFFECT DISORD. 2012 SEP;140(1):66-74
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STUDY RESULTS:

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ENROLLED= 150 → 19 DROPOUTS (6 = TEAEs) → COMPLETED = 131

WEEKS	1	4	8
VORTIOXETINE	10 to 20 mg (38)	20 mg (33) 20 to 10 mg (3) Withdrawn (2)	20 mg (51%) Mean Dose: 15.3 mg/day

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STUDY RESULTS:

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WEEKS	1	4	8	
ODQ TOTAL SCORE	-9.6 (1.6)	-21.2 (1.8)	-29.8 (1.9)	(p <0.0001)
NOT CARING	-1.4	-3.9	-6.0	(p <0.0001)
EMOTIONAL DETACHMENT	-1.0	-3.1	-4.7	(p <0.0001)
POSITIVE REDUCTION	-2.6	-5.6	-7.8	(p <0.0001)
GENERAL REDUCTION	-2.3	-4.5	-6.6	(p <0.0001)
ANTIDEPRESSANT AS CAUSE	-2.5	-4.3	-5.1	(p <0.0001)

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STUDY RESULTS:

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- At week 8: 50% of all patients reported no emotional blunting in answer to the "gold standard" standardized screening question ---->
- versus 100% at the beginning of the study

EMOTIONAL BLUNTING QUESTION:

- "Emotional effects vary, but may include, for example, feeling emotionally 'numbed' or 'blunted' in some way; lacking positive emotions or negative emotions; feeling detached from the world around you; or 'just not caring' about things that you used to care about. Have you experienced such emotional effects during the last 6 weeks?".

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STUDY RESULTS:

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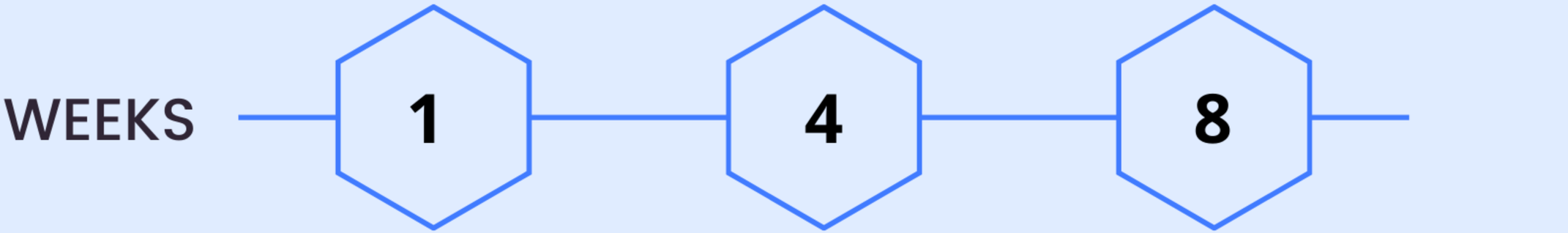

MADRS ANHEDONIA FACTOR SCORE:

-2.2 -5.9 -8.9 ($p < 0.0001$)

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STUDY RESULTS:

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Motivation and Energy Inventory (MEI):

- Significant from week 4.
- Across all subdomains: cognitive and mental energy, social motivation, and physical energy.

Cognitive Performance (DSST) Score:

- Observed at week 1 (4.3; $p<0.0001$)
- Increased by week 8 (7.8; $p<0.0001$)

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STUDY RESULTS:

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Overall Functioning (SDS):

- Observed for the total score as well as the single items.
- Most pronouncedly in the work/school domain.

MADRS Total Score (Depression Resolution):

- Improved significantly from week 1 to week 8.
- Rates of response at week 8: 61.8%.
- Rates of remission at week 8: 46.6%.

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WHAT CAN WE INFER NOW?

(1)

Patients with MDD who experienced inadequate depressive symptom resolution and emotional blunting after treatment with an SSRI or SNRI reported significant improvement after 8 weeks of treatment with vortioxetine 10-20 mg/day in:

- Emotional blunting,
- Overall functioning
- Motivation and energy,
- Cognitive performance, and
- Depressive symptoms

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WHAT CAN WE INFER NOW?

(2) This Positive effect on emotional blunting was observed **after just 1 week** of treatment.

(3) Improvement in **emotional blunting** with vortioxetine was strongly and significantly correlated with improvements in **motivation and energy**, and **overall functioning** ---> and **not mediated by** improvement in **depressive symptoms**.

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VORTIOXETINE MECHANISM?

- Mediated by modulation of cognitive control
- Lower serotonin transporter (SERT) occupancy than SSRIs

5 HT-3 BLOCKAGE

SERT BLOCKAGE

5HT-1A STIMULATION (where 5-HT neurons connect with glutamate and GABA neurons)

- Enhances the output of glutamatergic pyramidal neurons.
- Reduces the output of GABAergic interneurons in the prefrontal cortex & hippocampus.

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