CRITICAL ANALYSIS PROBLEMS

MCQ MOCK EXAMINATION PAPER 2016

STIMULUS

THIS STIMULUS CAN BE REMOVED FROM THE EXAMINATION ROOM IF YOU WISH, BUT ALL THE MATERIAL IN IT IS ALSO IN THE MAIN QUESTION PAPER.

DIRECTIONS

To be used as a handout while answering questions.
Do not answer questions in this booklet.

Using the pencil provided, please mark your responses in the MCQ Paper booklet itself.

Critical Analysis Question 1 (20 marks)

Mood instability as a precursor to depressive illness: A prospective and mediational analysis

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Abstract
Objective: Mood instability (MI) levels are high in depression, but temporal precedence and potential mechanisms are unknown. Hypotheses tested were as follows: (1) mood instability is associated with depression cross-sectionally, (2) mood instability predicts new onset and maintenance of depression prospectively and (3) the mood instability and depression link are mediated by sleep problems, alcohol abuse and life events.
Method: Data from the National Psychiatric Morbidity Survey 2000 at baseline (N = 8580) and 18-month follow-up (N = 2413) were used. Regression modeling controlling for socio-demographic factors, anxiety and hypomanic mood was conducted. Multiple mediational analyses were used to test our conceptual path model.
Results: Mood instability was associated with depression cross-sectionally (odds ratio: 5.28; 95% confidence interval: [3.67, 7.59]; p < 0.001) and predicted depression inception (odds ratio: 2.43; 95% confidence interval: [1.03–5.76]; p = 0.042) after controlling for important confounders. Mood instability did not predict maintenance of depression. Sleep difficulties and severe problems with close friends and family significantly mediated the link between mood instability and new onset depression (23.05% and 6.19% of the link, respectively). Alcohol abuse and divorce were not important
mediators in the model.
Conclusion: Mood instability is a precursor of a depressive episode, predicting its onset. Difficulties in sleep are a significant part of the pathway. Interventions targeting mood instability and sleep problems have the potential to reduce the risk of depression.

Keywords
Epidemiology, major depression, affect, predictor, early intervention

Full details of the survey methods are available in the main survey report (Singleton and Lewis, 2003). In brief, the sampling frame was the 'English Small Area Postcode Address'. Adults living in private households were selected using population-based multi-phase probability sampling. Experienced survey interviewers identified private households containing at least one person. They used the Kish grid method to select at random one person in each household, ensuring that all eligible household members had the same chance of being selected.

Presence of a depressive episode according to the International Classification of Diseases–10th Revision (ICD-10) was assessed at baseline and at the 18-month follow-up using the CIS-R (Lewis et al., 1992). The CIS-R has a reliability between 0.74 and 0.91 (Lewis et al., 1992) and can be used to derive ICD-10 diagnoses by an algorithm.

Because of the comorbidity between anxiety and depression as well as the fact that anxiety disorders may predate a depressive episode by some time (Moffitt et al., 2007), we controlled for anxiety symptoms using the CIS-R anxiety score.

Table 1. The cross-sectional and prospective link between mood instability and depression.

	Odds ratio (95% confidence interval)	*t*	*p*>*t*
Cross-sectional association			
Unadjusted	11.48 [8.63, 15.26]	16.84	<0.001
Controlling for socio-demographic variables[a]	10.74 [7.84, 14.69]	14.87	<0.001
Controlling for anxiety and hypomanic mood	5.28 [3.67, 7.59]	9.01	<0.001
Inception of depression at 18 months			
Unadjusted	4.38 [2.26, 8.48]	4.39	<0.001
Controlling for socio-demographic variables[a]	3.09 [1.35, 7.06]	2.68	0.008
Controlling for baseline anxiety symptoms and hypomanic mood	2.43 [1.03, 5.76]	2.04	0.042
Persistence of depression at 18 months			
Unadjusted	1.14 [0.38, 3.40]	0.23	0.819

[a]Age, sex, marital status, employment status and ethnicity.

Table 2. Mediators of the association between mood instability and new onset depression.

Sleep problems, hazardous drinking, separation and problems with close friends and family as mediators of the effect of MI on new onset depression					
Effect	OR	Robust standard error	z	p>z	95% CI
Total	2.78	1.07	2.66	0.008	[1.31, 5.91]
Direct	1.98	0.80	1.70	0.088	[0.90, 4.36]
Indirect	1.40	0. 12	4.04	<0.001	[1.19, 1.65]
33.12% of the link was mediated					
Sleep problems as a mediator of the effect of MI on new onset depression					
Effect	OR	Robust standard error	z	p>z	95% CI
Total	2.93	1.07	2.95	0.003	[1.44, 5.99]
Direct	2.29	0.88	2.16	0.031	[1.07, 4.86]
Indirect	1.28	0.10	3.16	0.002	[1.10, 1.49]
22.99% of the link was mediated					
Problems with close family or friends					
Effect	OR	Robust standard error	z	p>z	95% CI
Total	2.78	1.06	2.70	0.007	[1.32, 5.85]
Direct	2.60	0.99	2.51	0.012	[1.23, 5.50]
Indirect	1.07	0.03	2.26	0.024	[1.01, 1.13]
6.48% of the link mediated					
Sleep and problems with close family or friends as mediators of the effect of MI on new onset depression					
Effect	OR	Robust standard error	z	p>z	95% CI
Total	2.78	1.05	2.71	0.007	[1.33, 5.83]
Direct	2.06	0.82	1.83	0.068	[0.95, 4.48]
Indirect	1.34	0.10	3.84	<0.001	[1.16, 1.57]
29.18% of the link mediated: sleep (23.05%), problems with family/friends (6.12%)					

MI: mood instability; OR: odds ratio; CI: confidence interval.
Data were weighted, and controlled for age, gender, ethnicity, marital and employment status. Direct effect: the effect which is attributable to the direct association between mood instability and depression. Indirect effect: the part of the total effect between MI and depression explained by the mediating variables.

Critical Analysis Question 2 (20 marks)

Sodium valproate for the treatment of Tourette's syndrome in children: A systematic review and meta-analysis

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Keywords: Sodium valproate, Tourette's syndrome, Children, systematic review

A B S T R A C T

The aims are to evaluate the efficacy and safety of sodium valproate for children with Tourette's syndrome (TS). We searched PubMed, EMBASE, the Cochrane library, Cochrane Central, CBM, CNKI, VIP, WANG FANG database and relevant reference lists. Five RCTs ($N=247$) and five case series ($N=163$) studies were included. Only one RCT (93 patients) evaluated total YGTSS scores and there was significant difference in the reduction of total YGTSS scores between sodium valproate and the control group (3.50 ± 4.59 vs 7.86 ± 7.03, $P<0.01$). One RCT (30 patients) evaluated motor and vocal tics, and there was significant difference in the reduction of motor and vocal tics scores between sodium valproate and haloperidol (10.45 ± 4.15 vs 14.92 ± 3.01, $P<0.01$). Meta-analysis of three RCTs ($N=124$) showed there was no significant difference in the reduction of the number of tics between sodium valproate and the positive control group [Relative Risk (RR)=1.09, 95%CI (0.92, 1.30), $P=0.30$]. The pooled proportion in five case series studies which used tics symptom improvement self-defined by authors was 80.7% (95% CI: 73.7–86.2, $I^2=0$). No fatal side effects were reported. In conclusion, based on the limited evidence, the routine use of sodium valproate for treatment of TS in children is not recommended. Further well-conducted trials that examine long-term outcomes are required.

Introduction (excerpt):

Positive results from some RCTs and case series studies indicate that sodium valproate may be beneficial for children with TS, especially refractory TS (Wen and Wang, 2012; Zheng et al., 2001; Zhao et al., 1997). Although there is no exact definition of refractory TS (Sassi et al., 2011), it is widely accepted as TS in which clinical symptoms are not relieved after treatment with conventional anti-TS medications (Porta et al., 2011). Sodium valproate is recommended as one of the treatment options for TS in China (The Branch of Pediatric Neurology of Chinese Medical Association, 2013), but other professional organizations do not recommend it. Consequently, we conducted a systematic review to evaluate the efficacy and safety of sodium valproate in treating tics in children with TS.

Selection of studies and data extraction:
Two reviewers (Yang and Zhang) independently screened the titles and abstracts of every record. Full articles were obtained when either information given in the title or abstracts conformed to the selection criteria outlined previously, or could not be ascertained due to limited information. To include studies, data were extracted independently by each reviewer and entered into a standardized form. Discrepancies were resolved by consensus.

Table 1
General characteristics of included RCTs.

References	Characteristics of participants			Interventions		Treatment period	Outcome measures indicators	Diagnostic criteria
	Age (years)	Sample (male%)	Comparability of baseline	Treatment group	Control group			
Wen and Wang (2012)	5–12	62 (53)	Comparable	Sodium valproate sustained release tablets (20 mg/kg/d, bid)	Haloperidol (2 mg/each time, bid or tid)	8 Weeks‡	Author self-defined tics symptom improvement (rate of clinical efficacy: tics symptom control ≥ 50%)	DSM-IV
Wu et al. (2010)	4–18	30 (18)	Unclear	Sodium valproate (20 mg/kg/d, tid)+ conventional therapy	Conventional therapy	12 Weeks‡	(1) YGTSS scale (motor and vocal tic) T^*: 10.45 ± 4.15; $C^\dagger$: 14.92 ± 3.01(2) author self-defined tics symptom improvement (rate of clinical efficacy: rate of progress in tics symptom ≥ 30%)	DSM-IV
Zheng et al. (2001)	6–18	93	Comparable	Sodium valproate (gradually increase dose, final dose: 400–600 mg/d or 15 mg/kg/d)+ conventional therapy	Conventional therapy	8 Weeks‡	(1) YGTSS scaleT^*: 3.50 ± 4.59; $C^\dagger$: 7.86 ± 7.03(2) author self-defined tics symptom improvement (rate of clinical efficacy: YGTSS < 10 scores)	DSM-IV
Wang (2002a)	6.17–13.33	26 (21)	Comparable	Sodium valproate sustained release tablets (10–15 mg/kg/d, gradually increase dose, maximum dose 15–20 mg/kg/d, qn)+haloperidol (6–12 mg/d, gradually dcrease the dose to 2–4 mg/d)	Tiapride (400–600 mg/d)+ haloperidol (6–12 mg/d)	2 Months‡	Author self-defined tics symptom improvement (rate of clinical efficacy: tics symptom control ≥ 50%)	DSM-IV
Wang (2002b)	5.25–12.83	36 (25)	Comparable	Sodium valproate sustained release tablets (10–15 mg/kg/d, qn)+ psychotherapy	Haloperidol (0.5 mg/each time, bid, gradually increase dose by 0.5 mg/3–4 day)+ psychotherapy	Unclear‡	Author self-defined tics symptom improvement (rate of clinical efficacy: tics symptom control ≥ 50%)	DSM-IV

CCMD: Chinese Classification and Diagnostic Criteria of Mental Disorders; DSM-IV: diagnostic and statistical manual of mental disorder-IV.
Rate of progress in tics symptom: (tics scores before treatment−tics scores after treatment)/tics scores before treatment.

* Treatment group.
† Control group.
‡ The time of outcome measure is in the end of treatment.

Table 3
Quality assessment of included RCTs.

References	Quality assessment					
	Random sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective reporting	Bias from other resources
Wen and Wang (2012)	Unclear	Unclear	Unclear	Low risk	Unclear	Low risk
Wu et al. (2010)	High risk	Unclear	Unclear	Low risk	Unclear	Unclear
Zheng et al. (2001)	High risk	Unclear	Unclear	High risk	Unclear	Low risk
Wang (2002a)	Unclear	Unclear	Unclear	Low	Unclear	Low risk
Wang (2002b)	Unclear	Unclear	Unclear	Low	Unclear	Low risk

(Prior extract repeated)

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Figure 2

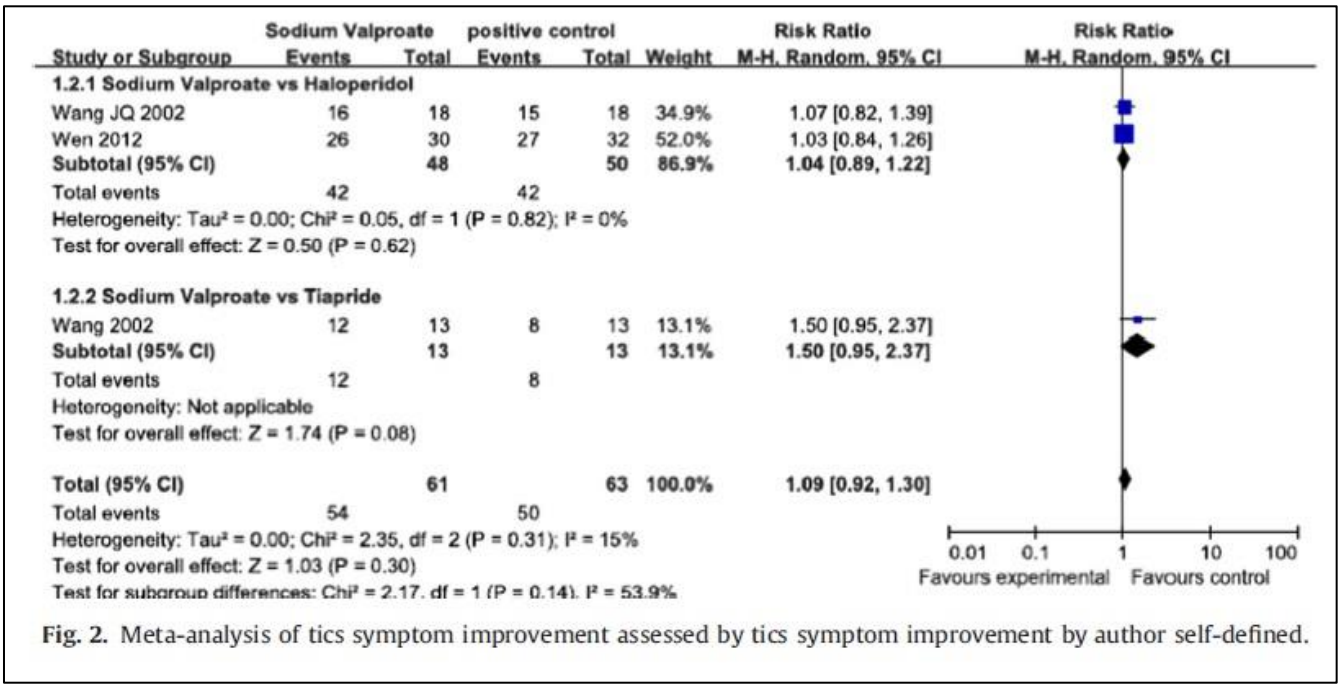

Fig. 2. Meta-analysis of tics symptom improvement assessed by tics symptom improvement by author self-defined.