### SCIENTIFIC VALIDITY

### Study Design

1. **Is the study approach consistent with research objective?**
   - [ ] Yes
   - [ ] No
   - [ ] NA

   **Problem identified:**
   The research objective was to investigate the association between abstinence prognosis and various statuses in pathological gamblers. There are several problems with the operational definition of abstinence in this study. Abstinence was defined only with respect to the one month period of assessment, and it is known that gambling addiction is "transient and episodic"...

   **Action recommended:**
   It is recommended that standard definitions of abstinence and relapse from the literature be used and groups not be grouped together. Further attempts to evaluate all the subjects should be made. Major revision and rethinking of the research design is needed...

   **Nature of revision**
   - [ ] Essential-Major
   - [ ] Optional-Major
   - [ ] NA

   **Relevant manuscript text (optional):**
   The present study tested the impact of Ig-LPS infection on the expression level of key proteins supporting foam cell formation, namely CD36, LOX-1, ACAT1 and ABCG1.

2. **Are the samples chosen appropriate?**
   - [ ] Yes
   - [ ] No
   - [ ] NA

   **Problem identified:**
   It is not clear how the outcome was determined—chart review or self-report? Was the history obtained from the medical chart obtained by someone who was blinded to the abstinence outcome?...

   **Action recommended:**
   The author should describe in detail in the manuscript introduction why these particular methods were used and then describe in detail what each parameter stands for.

   **Nature of revision**
   - [ ] Essential-Major
   - [ ] Optional-Major
   - [ ] NA

   **Relevant manuscript text (optional):**
   For quantitative outcome measures using repeated measures analysis of variance (mixed-effects model) for processing...

3. **Is the study missing any experimental controls?**
   - [ ] Yes
   - [ ] No
   - [ ] NA

   **Problem identified:**
   Positive controls are desirable for in vivo experiments. Since the authors test an anti-inflammatory activity of C38, a known anti-inflammatory drug (such as rolipram) could have been used.

   **Action recommended:**
   If the authors have data on positive controls for at least some experiments they could be included.

   **Nature of revision**
   - [ ] Essential-Major
   - [ ] Optional-Major
   - [ ] NA

   **Relevant manuscript text (optional):**
   Reconsider interpretation of the data on changes in uric acid, taking into account the differences in renal function changes seen in Groups A and B and Groups C and D.
Reporting Guidelines and Ethics

4. Is the article compliant with the appropriate reporting guidelines or checklist (STROBE, CONSORT, STARD, MOOSE, etc.)?

- Yes
- No
- NA

### Problem identified

Using STROBE criteria: Insufficient background information/rationale and description of setting, participants, variables, bias, statistical methods, and reasons for non-participation/handling of loss to follow-up. Questionable interpretation of results.

### Nature of revision

- Essential-Major
- Optional-Major

### Relevant manuscript text (optional)

It is assumed that for the emotional process related to Aad, it is highly possible that the recipient’s response in the form of the emotion generated...

5. Is appropriate research ethics information (consent, ethical approval, patient anonymity) provided?

- Yes
- No
- NA

### Problem identified

No mention of informed consent obtained in writing.

### Nature of revision

- Essential-Major
- Optional-Major

### Relevant manuscript text (optional)

Written informed consents from all subjects need to be included. Instead of patient’s family, mention that the consent was obtained from patient’s parents or guardians.

6. Has the sample been adequately described (number, inclusion and exclusion criteria, etc.)?

- Yes
- No
- NA

### Problem identified

Although subject characteristics are presented, there is very little information about inclusion/exclusion criteria. Consecutive adult outpatients over a specific 3-year period were used as subjects; however, the final sample size is very small (and we don’t know how many consecutive outpatients there were in this time period).

### Nature of revision

- Essential-Major
- Optional-Major

### Relevant manuscript text (optional)

The ankle brachial index (ABI) and toe brachial index (TBI) were measured by the same specially trained technician using the American Vista AVS Peripheral Vascular Diagnostic System...

7. Are the methods described in enough detail such that they can be replicated by other researchers?

- Yes
- No
- NA

### Problem identified

1) Quantitative evaluation of PSA (see above) is not described.
2) It is also unclear whether the CSB treatment was performed according to prophylactic or therapeutic model, i.e., whether animals were treated before or after full manifestation of OA (8 weeks). It is especially confounding, since in RT-PCR section it is stated “After the mice were killed, the arthritic joints of 5 mice from each treatment group in the therapeutic dosing model were removed”, implying that there was another treatment model used.

### Nature of revision

- Essential-Major
- Optional-Major

### Relevant manuscript text (optional)

DEHB diagnosis is determined by the specialist in child and adolescent psychiatry, according to DSM-IV criteria.