Metatheses of the Wernicke-Kleist-Leonhard research program

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Reply to Edward Shorter's comments

We feel honored and thankful to Mr Shorter for his comments (1) on our recent review of WKL achievements (2). We peculiarly appreciated the kindness and constructiveness of his critics. We are also very thankful to the INHN to give us the opportunity to clarify some points as it is clear from some remarks that we missed some of our goals in the writing of the paper.

As there are many points to discuss, we propose to post our responses not all at once, but one after the other. Let us start from a very basic philosophy of science answer to the remark about us:

> *"The authors are members of the Wernicke-Kleist-Leonhard Society, a group with an almost cult-like attachment to the nosology of Karl Leonhard."*

Mr Shorter is perfectly right in stating that we are all members of the Wernicke-Kleist-Leonhard International Society which might cast doubts on our goals and our impartiality.

This is an identity question: is our Wernicke-Kleist-Leonhard Society stuck in the past or is it pointing towards the future? The answer is not a simple yes/no statement.

Preserving traditional clinical skills

Members of our society embrace 3 commitments. The first two are: "*to preserve the tradition of clinical excellence in **differentiated psychopathology***"; and "*to promote, teach and diffuse knowledge and clinical skills in differentiated psychopathology*". Importantly, despite the name of our society our ambition is to embrace more largely any refinements in psychopathology and phenotypical proposals, in line with Prof. Helmut Beckmann's vision (3).

Though considering its precision and near-comprehensiveness, Karl Leonhard's classification remains our leading differentiated psychopathological framework (4). But, the preservation of Karl Leonhard's "tradition", should less be viewed as a "*cult-like attachment*", than a way to maintain the understanding of old texts and the departure of rephrased concepts from the originals.

This applies also to other reference frames. There is a need to be ***multi-lingual*** in order to understand the differences between these reading-grids. The importance of being multi-lingual is perhaps better appreciated by those of us who were first trained in the ICD-DSM framework before being interested in WKL and other traditions. We could measure how deep did these grids biased and limited our perception of patients' manifestations; the power of this imprint being even stronger than when the same labels are used to mean two very different things - the "periodic catatonia" point will be a perfect illustration of this.

Scientific objectives

Yet this article has been written in the perspective of our last commitment as members: "*to encourage, support and take part in scientific studies based on differentiated psychopathology*".

From a philosophy of science perspective, the society embraces most metatheses of ***dialectic critical realism*** (DCR, see ref. 5 for a review). While DCR postulate the existence of a mind independent reality, it also acknowledges that our access to it is indirect, and that our representations will remain incomplete and fallible, but hopefully also ***perfectible***. Hence, we fully agree with Mr Shorter when he is stating that the aim should be to develop a ***revisable***, rather than a "*cast in stone*", representations of psychiatric disorders.

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Our ontological realism and epistemological fallibilism are incompatible with any parochialism. Hence, we are fully in line with DRC's advocacy for the method of "***multiple working hypotheses***" (6).

In the field of psychoses, the decline of the DSM's categorical paradigm left room for a surge of alternatives proposals: DSM-5's dimensions (7), Hierarchical Taxonomy of Psychopathology (HiTOP) (8), Research Domain Criteria (RDoC) (9), Systems Neuroscience of Psychosis (SyNoPsis) (10), biotypes (Brain Research through Advancing Innovative Neurotechnologies)... The purpose of our review article was to remind that there still is room for classical biomedical approaches of which the WKL classification seems to us as the best illustration in our field.

The problem is that even the deepest understanding of these different reading grids, will not allow us to order their respective adequacy with reality. Because most the exclusive gathering of evidence according to a single framework; in post-positivistic terms, they will remain ***incommensurables*** (11). The only way to break this vicious circle would be to confront the verisimilitude of each proposal in the same ***adversarial collaborative*** (12) ***crucial experimental series*** (13). Our first attempt only challenged DSM's schizophrenia and tuned out to the advantage of the periodic catatonia and cataphasia distinction, but this was a proof of feasibility (14). Moreover, the idea is not to kill the less adequate models or paradigms, but rather to help them finding their weaknesses, give their supporters the opportunity to improve and perhaps to pick up ideas from the other models before the next experimental run. We take the opportunity of this response to encourage researchers interested in this approach to contact the first author. Indeed, we need ***dialectic*** argumentation with adversarial collaborators to help us in being ***critical*** with our models.

Hypotheses

Our core belief is that most of the psychoses are ***diseases***, i.e. "natural morbid entities" that take their categorical nature from their specific etiology or pathophysiology. We are also viewing these diseases as affecting one or several brain systems, hence anchoring our approach in systems neuroscience, systems biology and more widely in the emerging field of complex adaptive systems. We feel that this should not betray Wernicke's thoughts about brain functioning according to "psychic circuits" (15) following "diagram-kinds" of brain networks (16).

We believe that neither disorders, nor dimensions could accurately capture the real nature of psychotic entities. If psychotic symptoms result from the disfunction of one or several brain systems, they are expected to have ***power law distributions*** and to ***aggregate in definite clusters*** (17).

Why not dimensions?

This would be incompatible with current ***dimensional*** accounts which are based on normal distributions, i.e. implicitly assuming dimensions to result from the mere addition of many causes of very small effects. This is at odds with the misfunctioning of a system. Systems' dynamics depend on the evolving pattern of asymmetrical interactions (18). Even a single cause can have multiplicative effects resulting in the abnormally frequent emergence of rare events, e.g. positive symptoms, and/or destructive effects resulting in the abnormally frequent loss of others, e.g. negative symptoms. Normal distributions cannot account for these normally exceptional occurrences; Fat-tail distributions do (19).

Why not disorders?

Such rare symptoms are not supposed to occur in various combinations of equally meaningful symptoms in a list as for ICD-DSM ***disorders***. Rather, specific symptoms' clusters are expected to occur depending on the system(s) or the disordered domain(s). Yet their probability of occurrence is also conditioned by the context. The most regular should be the ones that directly result from the misfunctioning system(s), i.e. be primary symptoms (or "elementary" according to Wernicke) (20). Secondary manifestations depend on the context given by the macro-systems in which the disordered one(s) is(are) embedded, e.g. the whole central nervous systems and/or the physical or social environment of the patient.

But symptoms-complexes and phenotypes

This is why we keep on with the traditional biomedical paradigm: isolating and optimizing the description of ***symptoms-complexes*** and ***phenotypes*** and try to see if they can be the manifestations of ***syndromes*** or ***diseases*** (either simple or complex). It is clear to us that the strategy might fail. Our biggest fear would be that they would not be only 71, not even a hundred, but thousands of different very rare diseases in what we consider today as a schizoaffective spectrum. But our hope is that as in the field of mental retardation, beside the thousand of very rare diseases, they remain more frequent entities, like the fragile-X syndrome. In our mind, phenotypes like periodic catatonia or cataphasia are among the most credible candidate. But this is a bet, by no way a definitive statement.

As a matter of conclusion

"Yes", the identity of the Wernicke-Kleist-Leonhard International Society is rooted in the achievements of our forefathers. And, "Yes", we want to follow up their ambition in contributing to the deciphering the code of psychotic illnesses, even if it happens that we will have to refute some of their proposals and embrace the ones of others. There is no definite Truth, just temporary adequate representations; the most important is that some of them could translate into efficient therapies for our patients.

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