

Investigating the human locus coeruleus-norepinephrine system in vivo : discussions on the anatomy, involvement in cognition and clinical applications

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Propositions

• Propositions relating to the subject of the dissertation:

- "Segregation is disastrous for the whole human being. Man is a whole. You can't segregate him into pieces." M. Glezos. When studying brain and cognition, researchers tend to segregate the different parts in order to study the system of interest, but it is important to always return to the holistic level: from cell, to synapse, to neuromodulatory networks, to hormones secreted in the body.
- 2. Since the initial publication of the TSE scan sequence, numerous studies have used this scanning protocol for visualizing the LC in a variety of applications and have advocated its use as a diagnostic tool and biomarker. However, given the moderate reproducibility and scan-rescan stability of the TSE scan, clinical and longitudinal studies should be carried out carefully.
- 3. Our probabilistic atlas is the first probabilistic LC atlas and one of the few attempts to map the brainstem, a field that deserves more attention and promises to turn the brainstem from a "terra incognita" into a fully mapped and understood region.
- 4. Taking into consideration that lateralization effects play an important role in brain function, future studies should investigate whether our finding of structural LC lateralization can be replicated, and if this lateralization also exists for LC function.
- 5. MRI properties of a tissue are field-strength-dependent and the TSE sequence is SAR-intensive. Therefore, it is uncertain whether sequences that have proven successful at 3T, such as the TSE scan, will also provide the best contrast for visualization of the LC at higher field strengths.
- 6. The choice of control region has an influence on hemispheric contrast consistency. Depending on which control region is used, the correlation coefficient between the left and right LC contrast can vary substantially. This effect of control region should be taken into account when interpreting the various reports on hemisphere differences in LC intensity.

• Scientific propositions relating to the field of the subject of the dissertation:

- 1. tVNS is a newly developed method; more work is needed in order to evaluate its general and dose-dependent effects. Therefore we should be careful regarding its use, especially when it comes to clinical applications.
- 2. Researchers have a moral responsibility towards society and should be careful with the promises they make and conclusions they derive from their findings. This is of particular importance when it comes to clinical applications.
- 3. Conflicts of interest can be a carcinoma in academia. If we want to do good science and pursue the truth, researchers should be independent, and funding should originate from sources that do not in any way influence the results or benefit from the directionality of the results.
- 4. A researcher with substantial scientific knowledge but no genuine respect toward ethics and good conduct can be as dangerous as a child experimenting with an atomic bomb.

• Propositions on one or more subjects of the candidate's choice:

- 1. Applying the correct research methodology is important in fundamental research but can also solve societal dilemmas such as the huge dilemma "which is the best olive oil: the Greek or the Italian?" To answer this question, my friends and I carried out double-blind experiments involving a research committee and participants of Italian, Greek and other origin. Results indicate that the Greek olive oil rocks!
- "There is only one good: knowledge, and one evil: ignorance." Socrates. Academics have had the privilege to gain access to correct methodology and knowledge. It is their obligation to share this knowledge with the rest of society in order to help society prosper and leave behind every evil that stems from ignorance.
- As human beings we owe a single thing to ourselves: to reach our full potential, i.e. to become "καλὸς κἀγαθός" (the ideal of the complete human personality, harmonious in mind and body and ethical virtue).
- 4. For a better future in research, we should teach scientists to behave like Antigone, the famous character from the tragedy by Sophocles: they should learn to put principles of global, higher importance (e.g. search for the truth) above insignificant, secondary principles (e.g. secure a career).