Neuroinflammation in burnout patients

Deduction that in burnout patients, neuroinflammation exists;
model for measurement of neuroinflammation in burnout;
first physical measurement of burnout in history;
the perspective of burnout being an immunological reaction to emotional, non-somatic pathogens, 'emotional allergies'.

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Abstract. Neuroinflammation is a field that very rapidly increases in 2014. Not only diseases as AD (Alzheimer disease), but also a whole range of well know psychic illnesses can partly be explained by neuroinflammation. (Kuljis 2013, Iwata 2013). Burnout was first identified by dr. Freudenberger in 1974, and the first valid psychological test was crafted in 1986 (Christine Maslach, Maslach Burnout Inventory). Since 1986 burnout more or less had a 'standstill', until now. In this article a model for measurement of inflammation in burnout patients is conceived. The daunting perspective is that burnout consists of an IMNUMOLOGICAL reaction of body and mind without external, physical pathogen – just emotional 'allergy'

1. Burnout measurement 1986 – 2014

Burnout is usually measured by help of the MBI, Maslach Burnout Inventory (Maslach C. et al., 1986). A more modern, less known test is the SMBQ. Both models are validated in several scientific articles. In combination with the MBI the SCL-90 is usually used, in order to make sure no other psychich illness is 'leading' , other than possible burnout

2. Break-through deduction

Our deduction is that burnout shows neuroinflammation that is similar to cfs, chronic fatigue syndrome. In a psychological sense, the only difference between the two are:

1. in case of burnout, the cause can be related to work related situations, in which unrewarding experiences build up whilst the patient was not totally aware of them, and certainly did not take corrective action. 'All of a sudden', a state of burnout is reached, that is very close to chronic fatigue syndrome (cfs)

2. in case of burnout, burnout therapy, as performed by Stichting Burnout in its '12 steps program', leads – in almost all cases – to recovery. The 12 steps program is not easy to apply on chronic fatigue syndrome due to latter's lack of 'explaining situations' that can be called back and worked upon in therapy. For cfs, no convincing psychotherapeutic method is known.

Given the similarity of burnout to cfs, we deduct that neuroinflammation must be present in burnout patients approximately to the same extent as in cfs.

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Confirmation of neuroinflammation in burnout patients would be a breakthrough in the field of burnout:

- burnout could be proven by PET scans, showing neuroinflammation like in cfs (Nakatomi Y, Mizuno K., Ishii A. and Wada Y., 2014)
- but also, neuroinflammation could be REVERSED by non-pharmalogical intervention, like the 12 step burnout intervention program of Stichting Burnout.

The daunting perspective of burnout going along with 'neuroinflammation' is that burnout would be an IMMUNOLOGICAL reaction to a non-physical pathogen – namely an 'allergic, emotional allergy to circumstances'. Than can be state reversed by burnout recovery therapy.

3. Likely mechanisms to cause neuroinflammation in case of burnout

There are two candidate mechanisms for the generation of neuroinflammation in burnout:

a) overactivity of neurons. In the build op of burnout, it is typical an individual gives more input (energy) in order to meet 'deadlines'. When the external demands are not quite met, or the patient is still insecure whether demands will be met, he/she further increases its energy/input. At a certain point, further increase of energy input does NOT further improve the output (and/or rewards). As soon as the input is increased to the maximum, but the individual perceives the output indeed to drop, a kind of 'crash' occurs, after which the individual is 'suddenly burnout'. Most patients can recall this 'fall into burnout', and it takes usually place within 24 hours after realisation that further input is NOT possible and/or even leads to decreased output or success.

In the build of burnout, it is quite likely that neurons have been 'overactive', and that 'normal refractionary periods' of neurons have been breached.
To compensate for the functional loss, like in cfs/ME, patients exert greater effort to perform activities, resulting in enhanced neural activation (Ward N.S.,Brown M.M. And Thompsom A.J., 2003).

Overactivation of N-methyl-D-aspartate receptors results in production of proinflammatory cytokines, reactive oxygen species, and nitrogen species that cause inflammation (Frostegard J., Ulfgren A.K., Nyberg P. and Hudin U., 1999).

b) Direct impact of stress on the immune system and neuroinflammation. The other mechanism may be the immunologic responses to the initial infectious process, triggered by stress ONLY, without physical pathogens being present. (Grippo A.J. And M.A.K. Scotti, 2013; Boudsocq M. and Sheen J., 2013)

4. Novel burnout measurement 2014, including measurement of neuro inflammation

In our model of measurement of neuroinflammation in burnout, it is suggested that the 'cognitive impairment', that is usually agreed upon the case of burnout, is taken into account. Cognitive impairment is not taken into account in the MBI, but is in the SMBQ.
Our proposal is to use:

- the SCL-90 in order to scan for psychic illnesses in the broad sense, making sure no other psychic phenomenon is more important than burnout
- the MBI to measure burnout

In order to be complete and certainly include the cognitive impairment, the following tests are suggested in addition to above:

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- Visual Analogue Scale (VAS)
- Chalder Fatigue Scale,
- Center for Epidemiological Studies depression scale (DES-D)

So far it is ‘measurement from outside the ‘black box’, not taking into account neurobiological measurements of neuroinflammation caused by stress and burnout.

5. Additional neurobiological measurements

It is time to introduce novel neurobiological research findings in the field of burnout, especially the changes induced in the immune system and neuroinflammation caused by the burnout-related stress.

The impact of stress on the immune system and neuroinflammation has been well described buy Grippo and Scotti (2013). The measurement of neuroinflammation has been very convincingly proved by Nakatomi et al. (2014). Drawing on these findins, the following neurobiological method is proposed to measure the level of neuroinflammation in burnout patients.

We hereby propose the following neuroscientifical measurements for burnout on top of the earlier mentioned psychological measurements that dominated the last 38 to 40 years. Neurobiological measurements of burnout would introduce a new era of burnout research. The possibility to 'physically prove burnout' would help a great amount of patients, 'fighting' for recognition of their psychologically measured 'illness' in medicine.

5.1 Cytokine assay

In line with usueal cytokine measurement, it is proposed to apply C-®-PK11195 PET scan. Blood samples are coagulated at room temperature, to finally obtain sera. Sera are stored at minus 80 degree Celsius, and the measurement of the following cytokines is proposed:
- factor – alfa
- interferon –gamma
- interleukin-1-beta
- interleukin-6

5.2 PET scan

C-®-PK11195 is being injected after the start of the PET scan.

5.3 MR imaging

In parallel to the PET scan, MT images are coregistered.

6. Expected outcomes

Our expectations of outcomes is based on the deduction mentioned before.

Similar to cfs, it is expected :

- a very high correlation between ‘cognitive impairment score’ and BP ND of C-®-PK11195 (r=0,94, Nakatomi et al., 2014)
- a very high correlation between ‘CES-D’ score and BP ND of C-®-PK11195 (r=0,91, Nakatomi et al., 2014)

Furthermore it is expected that inflammation of the thalamus, particularly of the left intralaminar nucleus, is higher for burnouts than for controls, explaining the cognitive

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impairment.

Also inflammation of the amygdala is expected. Neuroinflammation in this area impairs cognitive activity through detoriation of the attentional function (Goupta, Paterson, Von Zweck and Lysaght, 2012).

The involvement of hypothalamus and amygdala means that burnout is linked to the limbic system. This is no surprise as many burnout patients, have, in the build up phase of burnout, become ***emotionally*** 'allergic' to some aspects of their work. The intuitive word 'allergy' is very well fitting in with the neurobiologically found 'neuroinflammation' as well as general impact on the immune system. It is also in aligment with the vision of Jerome Carroll, who described 'Staff burnout as a form of ecologycal dysfunction' in 1979.

For some physicians, burnout is close to depression. Burnout is more a depletion of energy, and depression is more 'anhedonia', but it would not be surprising that a lower energy level does not help to have a 'good mood'. We are curious whether burnouts will have significant neuroinflammation of the hippocampus in comparison to controls – one of the findings with cfs patients (Nakatomi et al. 2014).

In cfs/ME, patients complain somewhat more about pain than with burnout. It is interesting to observe how much functional interaction between the anterior part of the cingulated cortex and thalamus is taking place, in comparison to controls. Interaction mentioned is known to suppress pain (Harte, Spuz and Borszcz, 2010).

Last but not least, the relation between neuroinflammation and peripheral proinflammatory cytokines is promising. PET is a better measurement for neuroinflammation, than 'general cytokine meaurement' that also may reflect peripheral inflammation more than neuroinflammation. Above would be the first succesful attempt ever to measure burnout neurobiologically, after several failed attempts in neuroimaging burnout.

7. Conclusion

It is very much expected that burnout patients show significant neuroinflammation. The mechanisms involved, arguments, method of measurement and expected results are mentioned in above article. We are inviting laboratories with required facilities to carry out the proposed measurements. Confirmation of above expected results would be the first and biggest breakthrough in burnout research since 1986, due to the first succesful neurobiological measurements that would, to our expectation, indicate a significant higher level of neuroinflammation in burnout patients versus 'controls'.

But the 'deduction' in above article that:

'If chronic neuroinflammation in cfs patients exist → neuroinflammation will also be present in burnout patients'

is the first claim worldwide that burnout is PHYSICALLY MEASURABLE, and best through: measurement of neuroinflammation.

Burnout would turn out to physically consist of neuroinflammation, triggered off by 'emotional allergies' and not by external physical pathogens. The neuroinflammation would be reversible by good burnout recovery therapy and appropriate training as well as rearrangement of work circumstance so the allery has little chance of returning.

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