Clinical Neurophysiology 123 (2012) 1899–1900

Contents lists available at SciVerse ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Editorial

Heartbeat evoked potentials: A new possible clinical biomarker for depression based on the somatic marker hypothesis

See Article, pages 1950–1957

Since the annual costs of major depressive disorder (MDD) are continuously increasing worldwide (Greenberg et al., 2003; Bromet et al., 2011), the development of objective biomarkers for diagnosis and treatment of MDD should be an urgent issue. Although no objective measurements have been proven to be ready for clinical application as biomarkers for MDD, several brain functional measures, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), might be promising for future application (Leuchter et al., 2010). Especially, electrophysiological measures seem to be particularly practical biomarkers to help diagnosis and treatment of MDD because of their easiness, inexpensiveness and non-invasiveness (Leuchter et al., 2009).

In this issue of Clinical Neurophysiology, Terhaar et al. (2012) assessed the heartbeat perception score in sixteen depressed patients and matched healthy controls and found that the depressed patients showed less accurate heartbeat perception in comparison to the control group. They also measured heartbeat evoked potentials (HEP) by averaging EEG using ECG R waves as the trigger in both group. HEP were significantly reduced in depressed patients compared to controls, which was consistent with behavioral results of accurate heartbeat perception. Since mental exhaustion and reactive depression might be caused by lack of awareness of patients' body signal (Herbert et al., 2007; Mussgay et al., 1999), less accurate heartbeat perception and reduced HEP of depressive subjects in this study could be linked to various clinical bodily symptoms during depressive episodes. They concluded that HEP can be applied as the objective markers of altered bodily awareness and depression.

These clear results were obtained by combining sophisticated quantitative EEG (qEEG) analysis for evoked potentials. To minimize the overlapping volume-conducted electrical cardiac-field artifact contaminated in EEG recording, they applied independent component analysis (ICA) and current-source density (CSD) analysis and succeeded in improving the signal-to-noise ratio of HEP. They also adopted global field power (GFP) to avoid multiple testing and the subjective selection of single electrodes. This combination of ICA and CSD, GFP leads them to enhance the signal-to-noise ratio of their EEG data and find a new possible clinical biomarker for depression.

As they mentioned in their paper, according to the somatic marker hypothesis (SMH), difficulties in decision-making are related to reduce interoceptive awareness during depression (Damasio, 1994). The SMH proposed that emotion-based biasing signals arising from the body are integrated to regulate decision-making in situations of complexity. They also suggested that the observed lack of interoceptive awareness in depressed patients might contribute to a better understanding of various clinical symptoms during depressive episodes.

According to recent reviews and criticism of the SMH, one of the problems with this hypothesis is that previous studies of physiological responses accompanying decision making are still limited and restricted to findings through skin-conductance responses (SCR) (Dunn et al., 2006; Crone et al., 2004). In addition, since some researchers reported that the SCR is not a particularly sensitive index of an underlying emotion-based marker 'signal', SCR might not be the best objective measurement. Dunn et al. (2006) suggested that other sources of bodily feedback, such as facial muscle activity with electromyography (EMG) or heart rate with electrocardiogram (ECG) should be the next candidates for a somatic marker.

Although, as the SMH suggests, many studies has clarified that bodily states are substantially associated with decision making, the causal relationship between brain activity, bodily states and decision making is still unknown. A recent study analyzing correlation between heart rate variability (HRV) and simultaneously-recorded positron emission tomography (PET) during a simple stochastic decision-making task revealed that the rostral portion of the anterior cingulate cortex (ACC) might be responsible for the top–down regulation of peripheral physiological responses (Ohira et al., 2010). They suggested that peripheral physiological responses modulated by the brain can be conveyed to the brain and can affect decision making. Ohira also revisited the SMH and suggested that emotions and bodily states should be delicately modulated on the basis of evaluation of current situations in decision making (e.g., uncertainty) by the brain (top–down regulation), and then the modulated emotions and bodily states might in turn affect the next trial of decision making conducted by the brain (bottom–up feedback) (Ohira, 2010). We could reconsider the SMH by focusing on these bidirectional influences between the brain and body accompanying decision making.

Cardiovascular responses indicated by blood pressure, heart rate, ECG and HEP could be the new candidates for an objective marker of the SMH instead of SCR. Especially, HEP reported in Terhaar et al. (this issue) could be quite promising for the new objective marker reflecting the bidirectional brain and body interaction. Since we can visualize the current source density distribution and the functional connectivity by the whole head EEG recordings (Canuet et al., 2011), HEP refined by the combinations of sophisticated qEEG

1388-2457/$36.00
http://dx.doi.org/10.1016/j.clinph.2012.03.002

analysis might allow us to observe the direct link between peripheral cardiovascular responses and electrophysiological brain activity easily, inexpensively and non-invasively.

Finally, it is important to highlight the fact that the HEP in this study, a new type of somatic marker, shed light on the abnormality of brain-body interaction in depressed patients. It may be no exaggeration to say that this would be a milestone not to be missed in expanding the boundary of clinical application of electrophysiological methods in psychiatric fields.

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Terhaar J, Viola FC, Bar KJ, Debener S. Heartbeat evoked potentials mirror altered body perception in depressed patients. Clin Neurophysiol 2012;123:1950–7.

Ryouhei Ishii
Department of Psychiatry,
Osaka University Graduate School of Medicine,
D3 2-2, Yamada-oka, Suita,
Osaka 565-0871, Japan
Tel.: +81 6 6879 3051; fax: +81 6 6879 3059
E-mail address: ishii@psy.med.osaka-u.ac.jp

Leonides Canuet
EuroEspes Biomedical Research Center, Institute for CNS disorders and Genomic Medicine, Santa Marta de Babio, Bergondo 15166, La Coruna, Spain Tel.: +34 981 780 505; fax: +34 981 780 511
E-mail address: leocanon2002@gmail.com

Available online 11 April 2012