**Biological Testing for Suicidality: Can We Detect Suicidal Individuals?**

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**Background**

Early detection of suicidal behaviour is important for patient recovery and quality of life. Detecting people in acute crisis is also important. However, the etiology of suicide is multifaceted\(^1\), and any current predictive markers and tools are not specific for suicide, except a previous suicide attempt\(^2\). Any biological test attempting to assist in regular clinical assessment of suicidality would have to be highly sensitive (no false negatives) to avoid missing suicidal patients, but also preferably highly specific to avoid false positive results which cause undue stress to patients and families as well as unnecessary costs to health care systems. In this literature study we review current knowledge of biological tests and markers of suicide, specifically attempting to find methods that could be used in average clinical settings.

**Methodology**

A systematic literature search of publications in English without any publication time constraints was performed in Scopus, PubMed, and Web of Science databases. Search terms used in the title search field were: suicide*, test*; combined with terms in all search fields: biology*. The titles and abstracts of the articles found in these searches were scanned and duplicates eliminated. Reference lists of articles found through the searches were also scanned for additional articles. Relevant articles were obtained and a synthesis made.

**Results**

**Markers in blood and other body fluids**

Cerebrospinal fluid (CSF) measurements of 5-HIAA, HVA, and MHPG (metabolites of serotonin, dopamine, and noradrenaline, respectively), can be used to investigate central levels of these neurotransmitters, and their concentrations were negatively correlated to suicide attempt lethality in a small scale 2-year prospective study of people with bipolar disorder\(^3\), and several prospective studies have found that after an index suicide attempt, low CSF 5-HIAA predicts future attempts\(^4\). However, CSF sampling is more invasive and uncomfortable for the patient than taking blood samples. Peripheral serotonin activity can be used as a marker of central activity, and titrated imipramine binding to platelet serotonin transporters can be used to detect patients with low serotonin activity and possible suicidal intent\(^5\).

Neuropathic BDNF can also be measured from blood samples, but so far little is known about how well these levels describe cerebral concentrations\(^6\). Low levels of serum BDNF are associated with depression\(^7\), however some studies have found BDNF level differences between suicide and non-suicidal depressed patients\(^8\), while others have found no such difference\(^9\).

Measuring blood cortisol (the human stress hormone) for suicide “testing” has also been suggested, as it can show abnormalities in HPA function\(^10\). This blood test, taken at a specific time of day, would be a simple assessment tool. However, cortisol is not specific to suicide but can be elevated for many other reasons as well, but in a specialised patient setting its usefulness could increase. Measuring testosteron and oestrogen levels could be useful, as oestrogen is anxiolytic in normal physiological levels\(^10\), and low testosteron was found in a group of male suicide attempters, and the higher lethality of the attempt was, the lower the testosteron levels\(^11\).

**Functional tests**

The dexamethasone suppression test (DST) measures glucocorticoid receptor-mediated negative feedback of the HPA axis, and non-suppression in the test may be predictive of future suicidal behaviour even up to decades later\(^12\), and therefore useful as an aide for clinicians deciding on therapy options for patients suspected to have suicidal intentions\(^13\). If the DST response is abnormal, the HPA axis does not function properly. The DST does not seem to function universally in all patient settings, as some studies have failed to see any differences between suicide completers and controls while others have found non-suppressed DST associated with higher suicide risk\(^14\). Another functional test can be done with D-fenfluramine, which releases serotonin into synaptic clefts and inhibits its reuptake, thereby increasing prolactin hormone level\(^15\). If serotonin function is impaired as in e.g. suicidal states in schizophrenia, a lower prolactin response is observed. Both of these tests require relatively long observation periods (several hours) before results are obtained, which may make them unsuitable for brief patient contacts in outpatient clinical settings.

**Structural changes in the brain**

The structure of the brain may be altered in depression and with Magnetic Resonance Imaging (MRI) scans may reveal abnormalities such as white matter or gray matter hyperintensities\(^16\). However, MRI may not be available in regular clinic settings.

**Genetic markers**

Many have been searching for genetic markers of suicide, and several genes have been implicated. Heritability of certain psychiatric conditions such as depression, and increased familial suicide risk suggest a genetic element in the development of suicide behaviour\(^17\). However, studies have mainly focussed on specific genes related to serotonin signalling, and produced results that could not be replicated\(^18\),\(^19\). The serotonin transporter 5’ promoter region (5-HTTLPR) polymorphism “short” variant has been found to be associated to suicide in meta-analysis studies, but only in Caucasian samples, so racial genetic variation may complicate interpretation of results\(^20\). Screening the whole genome in a large number of studies has not yielded reproducible results that are still available. SNPs associated with suicidality has identified SNPs, which may be useful in genetic screening for suicide risk\(^21\). Three such SNPs are in genes coding for serotonin 5-HT1E receptor, glutamatergic alpha-2-actinin protein, and the pi subunit of the GABA-A receptor. Such SNP tests could easily be developed into routine assays, however their suitability to different patient samples needs to be established with different methods. Target genes for research into suicide genetics should be chosen more methodologically to improve outcomes of research projects\(^22\),\(^23\), and ethical considerations inherently involved in genetic testing need to be addressed.

**Conclusions**

Protein and other markers in body fluids can be used to estimate neurochemical processes in the central nervous system. However, they only reflect a cross-sectional view of the whole system, possibly pathologized, already prevailing in the body, while genetic markers could potentially identify vulnerable people even before they engage in suicidal behaviours. Any “preventative treatment” options for such individuals would be a matter for future development, as corrective gene therapies are still in developmental stages. However, people with an actively pathological state could be targeted for currently available treatments such as psychotherapies and medications. Despite a large number of studies over decades and much funding there are still many shortcomings, as there is still not enough little reliable, reproducible results available about many biological markers. Our understanding of the neurobiological mechanisms of suicidality is still limited, and therefore available markers are limited as well. Also, no currently available single biological marker alone can reliably predict suicidality, and biological tests are not currently in routine clinical use. Results need to be carefully considered in the correct clinical context with other observations, and even then there are possibilities for misinterpretations. Comparing results from several biological markers might reduce sensitivity and increase the costs of testing, the potential for methodological errors. As more research is being done on genetic markers of suicidality, and proteomics will enable investigating the activity of the whole proteome of the brain in different pathological states, we may be able to detect suicidal individuals more reliably by biological means.

References