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## EDITORIAL

### What have we learned from research into first-episode psychosis?☆



### ¿Qué hemos aprendido de la investigación en primeros episodios psicóticos?

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A new stage in the conceptualisation of schizophrenia has begun. It is defined by greater optimism for the future for those who suffer from this disease, a future that is less damaging and fatalistic as the one postulated up until very recently.

Today psychiatry stands in the middle of a crossroads. Research has achieved great advances and the time to consolidate an important qualitative change in the vision of psychiatric disorders in general and schizophrenia in particular has arrived. Proposals such as those in the controversial new edition of the DSM5<sup>1</sup> or positions such as that of Jeffrey Lieberman, President of the American Psychiatric Association, call for the same thing.<sup>2-5</sup> The vertiginous accumulation of new facts and evidence being incorporated progressively into clinical practice has led to a wave of renewal. We colloquially label this new stage with the “re” in schizophrenia, there having been new initiatives of reformulation, reconceptualisation, reassessment and even new proposals for alternative names or for renaming the disorder in the last several years,<sup>6-9</sup> which are added to such “classic” ideas like that of Colodrón.<sup>10</sup>

This new paradigm<sup>11</sup> attempts to approach the main areas of dispute that have to be overcome in research on schizophrenia: especially the clinical heterogeneity and the variability of research designs that make it impossible to achieve a global vision that combines the sheer volume of evidence that research teams around the world are generating, year after year in ever-growing amounts,<sup>12</sup> but that all too often lack this integrating vision.<sup>13</sup>

As Kapur, Philips and Insel (the last of these is currently the director of the National Institute of Mental Health in the USA) maintain, this bias or improper selection of the study samples is one of the main motives why biological psychiatry is taking so long to find valid and applicable clinical tests.<sup>14</sup> The emphasis should centre on identifying homogeneous subtypes, using longitudinal studies that employ standardised assessments and allow sharing and comparing among different trials.<sup>14,15</sup>

Carrying out longitudinal studies in the early stages of schizophrenia, with the first-episode psychosis (FEP), identified as such, is especially important. It avoids the effect of confounding variables such as the influence of antipsychotic treatment or chronicity, factors well known as provokers of long-term structural changes and that can explain part of the inconsistency of the findings obtained to date.<sup>16</sup>

Consequently, individuals with FEPs constitute an excellent group to use for studying the risk factors linked to the development of the disorders related to schizophrenia.<sup>12,17</sup> Studying this more homogeneous population increases the validity of the findings and makes it possible to obtain

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appropriate biomarkers for early diagnosis and for monitoring response to a therapeutic intervention or the evolution of the disease.

In our recent past, research on this population has allowed our group (along with others) to characterise a series of biomarkers, including the presence of an abnormal tolerance to glucose and diabetes,<sup>18–20</sup> of metabolic syndrome<sup>21</sup> and of telomere shortening and increase in pulse pressure.<sup>22</sup> These biomarkers would indicate the presence of an acceleration in the ageing processes,<sup>23</sup> explaining (at least in part) the decrease in life expectancy that these patients suffer with increased cardiovascular mortality.<sup>24</sup>

European and American groups, by means of large longitudinal studies on populations with FEP, have also been able to establish relevant findings, such as the presence of progressive neuroimaging changes,<sup>25</sup> establishment of predictors of recovery in follow-ups of up to 10 years<sup>26</sup> and the advantages of antipsychotic treatment that is adequate<sup>27</sup> and early.<sup>28</sup>

Over the last year the initial results of the FEP Project have been coming out.<sup>12</sup> This project involves a multi-centre, naturalistic, prospective, follow-up study designed to assess clinical, neuropsychological, biochemical, genetic and neuroimaging variables in a sample that included 335 patients with an FEP in Spain paired by age, gender and social-economic level with 253 healthy control subjects. The project is funded by the Spanish public health system through the Health Research Foundation (FIS [Spanish acronym]) and includes the participation of 16 Spanish centres, 14 of which are members of the Biomedical Research Networking Centre in Mental Health (CIBERSAM), ([www.cibersam.es](http://www.cibersam.es)).

The FEP Project has provided a description of a loss of pro- and anti-inflammatory balance,<sup>29</sup> as well as of an alteration in the regulation of the peripheral endocannabinoid system.<sup>30</sup>

The experience accumulated during all these years in research with first-episode psychosis, accompanied by the achievement of promising results and biomarkers, allows us to share a hopeful perspective. In the coming years, which will probably be very exciting in this area, the research will yield results that have effects on changes relevant to the conceptualisation, diagnosis, approach and prognosis of a disease as complex and challenging as schizophrenia.

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