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Breakthrough psychosis under antipsychotic maintenance treatment and social stress

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Rubio *et al.* (2019) demonstrated that breakthrough psychosis under antipsychotic maintenance treatment (BAMM) occurred in over 31% of a cohort representing the entire Finnish population. Based on available variables, they found associations with the instability of illness at the beginning of treatment episodes. Medication adherence was determined by proxy variables; individual information on the patient's state and situation was not available. Taking into account the high impact of rehospitalizations on the individual course of illness and the considerable economic burden of these treatment episodes, it is highly desirable to invest more research efforts than has been done so far to explore the reasons of BAMM in more detail. We investigated a much smaller sample of $N = 160$ hospital readmissions with schizophrenia, but conducted interviews with treating physicians and patients as well in those with BAMM referring to their opinions about the reasons of rehospitalization. Serum levels of prescribed antipsychotics and mood stabilizers (if prescribed) were determined in all readmissions at the next morning after admission. Patients were classified as adherent if the serum level of all medications was found within the reference range as indicated by the laboratory. Patients with depot medication were also classified as adherent if they had received their last injection on time. The remainders were classified as non-adherent. Table 1 displays differences between the 65 (40.6%) subjects classified as adherent and accordingly having BAMM and the others with insufficient serum levels. The latter had significantly more positive and general but not negative symptoms were more frequently involuntarily admitted and had a migration background.

In those patients with BAMM confirmed according to drug serum levels, treating physicians indicated the following reasons as 'probable' or 'possible' for the readmission in order of frequency: increase of psychotic symptoms (88%), increase of social stress (80%), increase of non-psychotic symptoms (45%), danger to others (36%), danger to self (35%), reasons on the part of the treating physician (e.g. dose changing, drug replacement) 27%, substance abuse 18%, somatic illness 15%.

Among the patients with BAMM, the majority ($N = 37$, 57%) acknowledged a causal association of their illness and the readmissions, the others denied an association or denied the illness. About one-third ($N = 22$, 34%) indicated reasons for the deterioration of their mental state: conflicts with fellow mentally ill people ($N = 6$), conflicts with relatives ($N = 4$), medication change in accordance with doctor ($N = 3$), working place conflicts ($N = 2$), work stress, divorce, alcohol consumption, somatic illness, illness of relatives, death of a close person, non-psychotic symptoms, loss of social contacts (each 1).

Table 1. Differences between adherent and non-adherent patients at re-admission

	Adherent	Non-adherent	Total	*p*
N	65 (40.6%)	95 (59.4%)	160	
Female	37 (57%)	45 (47%)	82 (51%)	
Involuntarily admitted	8 (12%)	34 (36%)	42 (27%)	<0.01
Migration background	9 (14%)	33 (35%)	41 (26%)	<0.01
Having a regular job	8 (12%)	19 (20%)	27 (17%)	
Living in partnership	14 (22%)	17 (18%)	31 (19%)	
PANSS total score	80 (s.d. 14.2)	87 (s.d. 14.1)	84 (s.d. 14.6)	<0.01
PANSS positive score	18 (s.d. 5.5)	23 (s.d. 5.0)	21 (s.d. 5.7)	<0.01
PANSS negative score	22 (s.d. 6.5)	22 (s.d. 5.7)	22 (s.d. 6.0)	
PANSS general score	39 (s.d. 6.3)	42 (s.d. 6.4)	41 (s.d. 6.5)	<0.01
Last hospital discharge (months)	25 (s.d. 34.87)	26 (s.d. 25.11)		
Duration of illness (years)	19 (s.d. 8.19)	18 (s.d. 11.02)		

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To our mind, some conclusions can be drawn: (1) Patients with BAMM have considerably less severe positive and general symptoms at admission than non-adherent patients. The reason could be that even in BAMM patients, antipsychotics have some protective efficacy. (2) There is a considerable agreement between physicians and patients, that interpersonal conflicts, or respectively, in a wider sense, social stress, plays a major role in the origin of relapse and rehospitalization. It is unclear whether increased stress is the origin or consequence of increased symptoms. (3) The role of general psychiatric symptoms in the origin of relapses might have been underestimated and under-researched so far.

It is well known for long times that social stress (urbanicity, expressed emotions, victimization) plays an important role in the origin of schizophrenia (Matcheri *et al.*, 2008). However, the etiological factors in relapses have much less been scrutinized. Limited work indicates the nature of neurobiological mechanisms (Remington *et al.*, 2014) and epidemiological and social factors associated with relapses (Doering *et al.*, 1998; Alvarez-Jimenez *et al.*, 2012; Boaz *et al.*, 2013; Alphs *et al.*, 2016). Research on what happens at the time of relapse is widely lacking. We please that future research should focus on the micro-mechanisms leading to relapses, particularly on the causal and timely interactions of stress and symptoms. This could offer windows of opportunity for therapeutic interventions of behavioural as well as pharmacological nature.

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