‘Psychopathological differences between Asperger syndrome/normal IQ, no language impairment autism spectrum disorder and schizotypal disorder in an adult sample’

Introduction
The purpose of this study is to identify psychopathology (psychiatric symptoms) that can differentiate between Schizotypal Disorder (SD) and Asperger Syndrome (normal IQ, no language impairment Autism Spectrum Disorder) (ASD) in young adults. With our present knowledge, the differentiation between ASD and SD can be difficult, as they both present with social difficulties, odd (but not psychotic) behaviour, and a ‘feeling of not being as everyone else’ (1).

Background
SD is a non-psychotic disorder within the Schizophrenia Spectrum (in ICD-10) (1, 2), and has a prevalence of 3.9 % in adult samples (3). Autism Spectrum Disorder, a pervasive developmental disorder (including Asperger Syndrome) (1), has a prevalence of 1 % (4).

SD is typically diagnosed in young adults, whereas ASD typically is diagnosed in childhood. However, the ASD symptoms sometimes first become invalidating in young adulthood, where social demands exceed the individual's capacity. In these cases, patients with symptoms corresponding to ASD, are also seen in Adult Psychiatry.

Unfortunately, the fact that ASD most often is diagnosed in Child- and Adolescent Psychiatry, together with ASD treatment being a municipal responsibility (and the Mental Health Service is not), makes the experience with seeing and diagnosing ASD in Adult Psychiatry scarce (5). Similarities between the two conditions, as stated above, are seen in both social dysfunction (2, 6, 7) and cognitive impairments (8), and studies suggest that patients presenting with symptoms corresponding to ASD in Adult Psychiatry, are either overlooked (9, 10), or diagnosed within the schizophrenia spectrum (9, 11). Whether this ‘mismatch’ occurs due to differences in diagnostic tradition, diagnostic inexperience with ASD in Adult Psychiatry, or in fact represents an overlap between the two conditions, is not yet fully explored (8).

Historically there has been an on-going debate regarding the correlation between ASD and schizophrenia spectrum disorder (6, 8). The debate is still present today, both in the everyday clinic and academically, as the topic recently is raised as a future focus area in the Schizophrenia Bulletin (12).

Diagnosis
It is highly relevant to refine the psychopathological description of the two conditions. A better understanding of what constitutes ‘the core’ of them both, significantly sharpens our differential diagnostic possibilities. As it is not possible to take a blood sample or a brain scan to aid psychiatric diagnosis, the description of present psychopathology is the only way to diagnose psychiatric illness. An accurate diagnosis is crucial for a relevant treatment and rehabilitation plan for the individual patient (13), as the diagnosis guides the help and support offered, both in the mental health services and in the municipal system.

Further, the biology of these conditions is not yet fully known, and to properly guide neuro-psychiatric research, high diagnostic accuracy is imperative (14, 15).
In the overall context of this study, both diagnostic domains are considered to be spectrum disorders, i.e., SD is considered as a non-psychotic disorder in the schizophrenia spectrum, and Asperger Syndrome as an early emerging developmental disorder, in the Autism Spectrum. However, as ICD-10 is the principal diagnostic system used in Denmark, ICD-10 will be the diagnostic point of reference in all available clinical material. Therefore this study will refer to the diagnostic criteria defined in ICD-10, when including participants.

**Altered self-experience**
Within the schizophrenia spectrum alterations in (self-)experience are known to be present (2, 16). These experiential alterations are described as a loss of first-person perspective (17, 18), i.e. for these patients the experience of him-/herself as a subject is disturbed. This means that the *form* and *structure* (rather than content) of the patients’ thoughts and experiences is altered (15).

These alterations are considered highly specific for the schizophrenia spectrum (16), and are therefore not thought to be present in equal amounts and/or distribution in ASD. If this assumption is true, an examination of anomalous self-experiences would be valuable to aid clinical differentiation between SD and ASD. However, equally important is if there would prove to be no significant difference in level of self-disorder, as this possibly would call for a revised diagnostic tradition (8).

**The patient’s own experience of illness**
Essential for characterizing the schizophrenia spectrum, is the patients experience of an altered existential pattern (the schizophrenic autism (19)), a *loss of natural evidence* (20, 21), that impregnates every aspect of the patients being (19, 22). By the patient, this is often described as a *change*, a new state, which is essentially different for how it was before. The examination of altered experiences enlightens this altered existential pattern, and describes how the patient experiences him- or herself, and his or her world.

The ASD diagnosis and research has long been guided by observed (rather than experienced) deficiencies in social interaction, communication and behaviour (the classic triade) (23, 24). In the later decades, the ASD research has shifted focus towards ‘lack of sense of central coherence’ (deficits in the ability to create meaningful contexts from information available in a given situation) (25), direction of thought (*self versus others*) (25, 26) and the lack of ability to predict other people’s beliefs, desires and intentions (*theory of mind*) (27). Still however, the ASD patients’ own experience is insufficiently described (28, 29).

**Aim, objectives and hypotheses**
The aim of the study is to do an in depth exploration of differences in present psychopathology (psychiatric symptoms) in young adults with SD and ASD. This will elaborate and refine our understanding of SD and ASD specifically, and both spectrum disorders in general.

The objectives are to;
1. Explore differences in psychopathology between young adults with SD and ASD and
2. Contribute to both the general and the specific (in SD and ASD respectively) description of the autism concept.

The hypotheses are that;
1. The total level of altered experiences (EASE total score (16)) is higher in SD than in ASD and
2. The pattern of most occurring altered experiences (individual EASE items) is different in ASD, compared to SD.
**Design, participants and methods**

The study is observational and comparative in design. 100 participants will be included; 50 diagnosed with SD and 50 with ASD.

**Inclusion criteria:**
- ICD-10 diagnosis of Asperger syndrome (F84.5) or infantile autism (F84.0) with normal IQ and no language impairments (1) or schizotypal disorder (F21) (1)
- Age 18-30 (both inclusive)

**Exclusion criteria:**
- Known non-verbal IQ < 80 (verbal IQ < 70) or an educational level corresponding to <9 years of primary education
- Diagnosed with both Schizophrenia Spectrum Disorder and Autism Spectrum Disorder
- Psychotic symptoms (< 1 day of duration, lifetime)
- Severe physical illness (life-limiting, or limiting interview capacity)
- Organic brain disorder (corresponding to ICD-10 chapter F00-09 (1))
- Active heavy alcohol or substance abuse (corresponding to ICD-10 definitions (1))
- Not fluent in the Danish language
- Legal patients

**Selection and expert panel**

Essential to the study, is recruitment of participants with typical symptoms, to reduce confounding of the results by diagnostic uncertainty. Thus we have chosen to recruit participants, from specialized units, who are already diagnosed. Participants with SD will be recruited from OPUS-teams (a specialized treatment program for patients with first episode of schizophrenia spectrum disorder), within the Mental Health Services in the Capitol Region of Denmark, and participants with ASD from The Danish Autism Centre (a non-profit organization for people with ASD) (30).

Possible subjects will be identified by diagnosis through patient registers, and informed consent will be obtained. The subjects’ medical records will then be revised, to further isolate subjects eligible for inclusion. From the medical records, described social and psychiatric history and observed psychiatric symptoms will be summarized for each eligible subject. The summary will be presented to an expert panel, which divides the participants into four groups: ‘participant with symptoms typical of AS’, ‘participant with symptoms typical of SD’, ‘participant with inconclusive/non typical symptoms’ and ‘non eligible participant’ to ensure the identification of subjects with typical symptoms, according to clinical consensus (based on the information available).

The use of an expert panel is imperative; to further ensure isolation of subjects with typical symptoms only. The panel consists of two senior psychiatric consultants (Peter Handest, Mental Health Center North Zealand, Denmark and Lena Nylander, Adult Psychiatry Lund, Sweden). The international representation significantly strengthens the generalizability of the project.
**Psychopathological examination**

All included participants are asked for a detailed social and developmental history, and interviewed with three *semi-structured* interviews:

1. *Schedules for Assessment in Neuropsychiatry (SCAN)* (31); An assessment of psychopathology and behaviour associated with the major psychiatric disorders in adult life.
2. *Autism Diagnostic Observation Schedule (ADOS), module 4* (32); An assessment of communication, social interaction and play (or imaginative use of materials) for adults who are verbally fluent, to identify symptoms within the autism spectrum.
3. *Examination of anomalous self-experience (EASE)* (16); A checklist for exploration of experiential anomalies, covering five domains: cognition and stream of consciousness, self-awareness and presence, bodily experiences, demarcation/transitivism and existential reorientation.

The Ph.D.-student will obtain social and developmental history, and carry out the SCAN and EASE interviews. The ADOS will be carried out by a consultant psychologist at The Danish Autism Centre.

All psychopathological interviews will be videotaped. A subset of the taped SCAN and EASE interviews will be co-rated by clinical supervisor Peter Handest. Co-ratings will also routinely be performed amongst psychologists at The Danish Autism Centre, who conducts the ADOS interviews.

**Self-administered scales**

The participants will be asked to fill out the following self-administered scales, concerning psychiatric symptoms and psychological well-being:

1. *The Autism Quotient (AQ)*. AQ is a 50 question scale, for the assessment of autistic traits, assessing the areas; social skill, attention switching, attention to detail, communication, and imagination. (ref)

2. *The Schizotypal Personality Questionnaire (SPQ)*. SPQ is a 74 item scale, for the assessment of schizotypal personality, assessing the areas; ideas of reference, excessive social anxiety, odd beliefs or magical thinking, unusual perceptual experiences, odd or eccentric behavior, no close friends, odd speech, constricted affect, suspiciousness. (ref)

3. *The WHO-5 Well-Being Index (WHO-5)*. WHO-5 is a 5 item scale, for the assessment of subjective psychological well-being.

**Other interviewer ratings**

1. *Global Assessment of Functioning (GAF)*. GAF is a numeric scale (1 through 100) for assessing social, occupational, and psychological functioning.

2. *The Clinical Global Impressions scale (CGI-Severity)*. The CGI-Severity is an assessment of the clinician’s global view of the patient’s severity of psychopathology on a 7 point scale.

**Statistical analyses**

The results will be analyzed quantitatively. To investigate between group differences, group wise comparisons between SCAN algorithms (relevant for the two diagnoses), ADOS algorithms and EASE outcomes will be applied. Further, secondary correlations across psychopathological domains will be explored, and explorative cross-diagnostic factor analysis will be performed (with the knowledge of possible limitations due to sample size).
**Ethical considerations**

Prior to inclusion a differentiated informed consent will be obtained from all participants;

1. An informed consent to participate in the study,
2. An informed consent to obtain relevant medical records, and the research group’s revision of the medical records,
3A. An informed consent to the recording of the interviews on videotape, including an informed consent to the storage of taped material.
3B. *An informed consent for the research group to use* the taped material for educational purposes.
4. An informed consent to be contacted after termination of the study if necessary, and to a possible 5 and 10 year follow up.

Only the consent to participate in the study, and the research group’s revision of medical records is mandatory for inclusion (1 and 2).

The study is approved by the Danish National Board of Health (Danish Patient Safety Authority) (Sagsnr. 3-3013-1564/1). All data handling will be performed according to approval from The Data Protection Agency (j.nr.: 2012-58-0004). As the study is interview-and observation based, an approval from The National Committee on Health Research Ethics is not required.

**Feasibility of the study**

The Danish Autism Centre is in contact with 50-100 users per year, and has a database with about 1000 former users, all with an ASD diagnosis. The centre has wide experience with participant recruitment from several former research collaborations. According to The Danish Psychiatric Central Research Registry, 938 patients with SD were in contact with the Danish Mental Health Services in 2012 (33). To achieve a least meaningful difference (LMD) of a total EASE-score of 10, a total of 16 participants in each diagnostic group is required (based on means and SD’s in Raballo et al (34)).

A total estimate of 100 included patients is considered the maximum feasible capacity, considering above described patient flow and the estimated duration of the inclusion period.

The office facilities and office material required for the study are made available at Mental Health Centre Ballerup, where the study is anchored. The social difficulties often present in the concerned patient groups, will require acquisition of portable video and sound equipment, so that interviews can be carried out wherever the participant is most comfortable.

**References**


