| CONCEPT PAPER TEMPLATE | |
|---|---|
| **Provisional Paper Title:** | Does schizotypy predict future suicidality? |
| **Proposing Author:** | Kirstie O'Hare |
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| **Date:** | |
| **P.I. Sponsor** (if the proposing author is a student or colleague of an original PI) | Richard Linscott |

**Objective of the study:**

*Schizotypy* is a schizophrenia liability state.[1] Its expression comprises a range of enduring characteristics that resemble subclinical features of schizophrenia. Indeed, the features of schizotypy and symptoms of schizophrenia have similar distributions of positive (cognitive-perceptual), negative (interpersonal), and disorganization components. Whereas schizotypy is often assessed using measures of psychosis-like experiences (PLE), PLE are but one component of the liability state.

Evidence suggests that components of schizotypy are associated with suicidal thinking and behaviour. For example, in a prospective study we found evidence that positive schizotypy in the mid teens predicted desire for death two years later[2]. Others have found similar evidence that positive, negative, and disorganized features of schizotypy are associated with a range of expressions of suicidality, from passive suicidal ideation to completed suicide, although most of this evidence was derived using cross-sectional designs.[3,4]

The best contemporary account of the link between schizotypy and suicide is problematic. As the reasoning goes, suicidality in schizotypy is caused by those environmental risk factors that cause psychosis and schizophrenia. However, environmental risk factors are correlational predictors and cannot be presumed to reflect causal processes. Second, some environmental risk factors are heritable and could be secondary to the schizophrenia genotype. Finally, evidence shows that a significant proportion of the variance in suicidal thinking and behaviour is uniquely associated with schizotypy and that schizotypy is associated with greater lethality.

Therefore, our overall objective is to examine whether schizotypy has a causal effect on the development of suicidal thoughts and behaviour. We seek to achieve this objective in two stages, the first of which is the focus of this application. In this first stage, we will compose measures of schizotypy and test whether these predict concurrent suicidal ideation and behaviour. Positive features of schizotypy could be indexed using DISC-C ratings of PLE, however DISC-C PLE ratings do not capture disorganization and negative components of schizotypy. Consequently, we will using item-level observer rating data to construct indices of schizotypy components, test the reliability and validity of these, and then subsequently examine the relationship of schizotypy indices with suicidality.

Subject to our achieving this objective, and depending on discussions that will be held between Poulton, Caspi and Moffitt about the Dunedin Study 'omics policy in mid-2017, we plan to later examine whether the schizotypy-suicidality association is moderated by genetic factors by using a Mendelian randomization approach.

**Data analysis methods:**

First, we will test whether items from the Quay & Peterson Revised Behaviour Problem Checklist (RBPC) can form a valid and reliable measure of schizotypy. Initial composition of schizotypy indices from the RBPC will be based on item content and alignment of item content with descriptions of schizotypy. Subsequently, the psychometric properties of these indices will be examined and poorly performing items will be removed. We will consider:

1. Internal consistency; test correlations of schizotypy-related items from RBPC with each other (age 13 and 15)
2. Test-retest reliability; test correlation of schizotypy-related items from RBPC at age 13 with the same items at age 15
3. Convergent validity; test correlations from schizotypy-related items from RBPC (age 13/15) with hallucination/delusion-related, diagnosis of schizophreniform disorder and use of services items from DIS (ages 18-38)
4. Divergent validity; test correlations from schizotypy-related items from RBPC (age 13/15) with eating disorder related items from DIS (ages 18-38)

Second, once indices of schizotypy have been finalised, we will test whether schizotypy is associated with increased risk of worst-point suicidal ideation (both passive and active) or attempts, using correlational and regression models

1. Passive ideation; test whether schizotypy score predicts items from DIS; (1) 'During the last year have you thought a lot about death (your own, someone else's or death in general)?' (2) 'Have you felt like you wanted to die?' (worst-point from ages 18-38)
2. Active ideation; test whether schizotypy score predicts item from the DIS: 'Have you felt so low that you thought about committing suicide?' or 'Did you think a lot about committing suicide?', item from the DSHI: 'In the past year have you thought about committing suicide?', item from the EASI: 'Have you thought about committing suicide' (worst-point from ages 18-38)
3. Attempts; test whether schizotypy score predicts item from the DIS: 'Have you attempted suicide?'(worst-point from ages 18-38)

**Variables needed at which ages:**

**Schizotypy**

Schizophrenia- and psychosis-related data, and diagnosis of schizophreniform disorder diagnosis from DIS (ages 13, 15, 18, 21, 26, 32 & 38). (Item-level data)

Data from the Quay & Peterson Revised Behaviour Problem Checklist (RBPC; ages 13 & 15). (Item-level data)

**Suicidality**

Suicide data from DIS (ages 18, 21, 26, 32 & 38). (Item-level data)

Data from the Empowerment Against Self-Hurt Interview (EASI; age 32). (Item-level data)

Data from the Deliberate Self-Harm Interview (DSHI; age 26). (Item-level data)

**Other**

Use of services data from DIS (ages 13, 15, 18, 21, 26, 32 & 38). (Item-level data)

Eating disorder data from DIS (ages 13, 15, 18, 21, 26, 32 & 38). (Item-level data)

**Significance of the study (for theory, research methods or clinical practice):**

The significance of the project rests largely on the outcome of the subsequent phase of this investigation, namely an examination of the influence of schizophrenia-related genotypes on suicidality outcomes. Evidence that suicidality is predicted by a schizophrenia gene risk score would inform future questions on the emergence of suicidality among those at risk for schizophrenia. First, it would suggest that greater leverage against suicide may be obtained by understanding the nexus of the developmental pathway for schizophrenia with psychological processes involved in the emergence of suicidality. Second, it would promote the tailoring of risk management strategies for those affected by schizophrenia. Third, better understanding of the nexus of psychological mechanisms involved in the pathways to schizophrenia and suicidality could inform new approaches to community-level preventive interventions.

**References:**


1. Lenzenweger, M. *Schizotypy and schizophrenia: The view from experimental psychopathology*. (Guilford Press, 2011).
2. Schimanski, I. D., Mouat, K. L., Billinghurst, B. L. & Linscott, R. J. Preliminary evidence that schizophrenia liability at age 15 predicts suicidal ideation two years later. *Schizophr. Res.* 8–10 (2016). doi:10.1016/j.schres.2016.08.030
3. Jahn, D. R., Devylder, J. E. & Hilimire, M. R. Explanatory risk factors in the relations between schizotypy and indicators of suicide risk. *Psychiatry Res.* **238,** 68–73 (2016).
4. Teraishi, T. *et al.* Relationship between lifetime suicide attempts and schizotypal traits in patients with schizophrenia. *PLoS One* **9,** e107739 (2014).
5. Honings, S., Drukker, M., Groen, R. & Van Os, J. Psychotic experiences and risk of self-injurious behaviour in the general population: a systematic review and meta-analysis. *Psychol. Med.* **46,** 237–251 (2016).
6. DeVylder, J. E. *et al.* Social and psychological contributions to the co-occurrence of sub-threshold psychotic experiences and suicidal behavior. *Soc. Psychiatry Psychiatr. Epidemiol.* **50,** 1819–1830 (2015).
7. DeVylder, J. E., Lukens, E. P., Link, B. G. & Lieberman, J. A. Suicidal Ideation and Suicide Attempts Among Adults With Psychotic Experiences. *JAMA Psychiatry* **72,** 219 (2015).
8. Kelleher, I. *et al.* Psychotic symptoms and population risk for suicide attempt: a prospective cohort study. *JAMA psychiatry* **70,** 940–8 (2013).
9. Mann, J. J. & Currier, D. A Review of Prospective Studies of Biologic Predictors of Suicidal Behavior in Mood Disorders. *Arch. Suicide Res.* **11,** 3–16 (2007).
10. Prinstein, M. J. Introduction to the special section on suicide and nonsuicidal self-injury: a review of unique challenges and important directions for self-injury science. *J. Consult. Clin. Psychol.* **76,** 1–8 (2008).

**Data Security Agreement** (customize as necessary)

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| Provisional Paper Title | Does schizotypy predict future suicidality? |
| Proposing Author | Kirstie O'Hare |
| Today's Date | |

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Please initial your agreement

My project is covered by Dunedin Study's IRB approval *OR* I have /will obtain IRB approval from my home institution.

I will treat all data as "restricted" and store in a secure fashion.

I will not share the data with anyone, including students or other collaborators not specifically listed on this concept paper.

I will not post data online or submit the data file to a journal for them to post.
*Some journals are now requesting the data file as part of the manuscript submission process. Data from the Dunedin Study cannot be shared because the Study Members have not given informed consent for unrestricted open access. Speak to Richie Poulton, DMHDRU Director for strategies for dealing with data sharing requests from Journals.*

Before submitting my paper to a journal, I will submit my draft manuscript and scripts for data checking, and my draft manuscript for co-author mock review, allowing three weeks.

I will submit analysis scripts and new variable documentation to DMHDRU data manager after manuscript gets accepted for publication.

I will return all data files to the PI responsible and/or DMHDRU Data Manager after the project is complete. The data remains the property of the Study and cannot be used for further analyses without express, written permission.

**Signature:**